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BRITISH MEDICAL JOURNAL

LONDON SATURDAY JULY 18 1953

British Medical Association

ONE HUNDRED AND TWENTY-FIRST ANNUAL MEETING, CARDIFF, 1953

President's Address

"WITH HEAD, AND HEART, AND HAND"

BY

J. W. TUDOR THOMAS, M.D., M.S., D.Sc., F.R.C.S.

Senior Ophthalmic Surgeon, United Cardiff Hospitals; Lecturer in Ophthalmology, Welsh National School of Medicine

It is with very sincere feeling that I wish to express my appreciation of the honour of being elected President of the British Medical Association, and my gratitude to my colleagues in the Cardiff Division, the Council, the Representative Body, and the Association for electing me to this high office.

In the list of Past-Presidents of the Association are to be found many honoured names, distinguished men, leaders of the profession, and pioneers in their work. Among them I am happy to mention my friend and colleague Sir Ewen Maclean, of Cardiff, who became President in 1928, when last the Association met in Wales. Names such as Stokes, Macewen, and Lord Dawson of Penn serve to indicate the quality of those who have in the past held the office of President of the Association. In recent years, as we know, that quality has been well maintained by medical men of great eminence.

Among the Past-Presidents five were ophthalmologists: Reeve, of Toronto (1906); Snell, of Sheffield (1908); Harvey Smith, of Winnipeg (1930); Sir James Barrett, of Melbourne (1935); and Dr. Sichel, of Capetown (1951). It is indeed an honour and a privilege to occupy an office which in the past has been held by such a number of notable and distinguished medical men.

May I now, on behalf of myself and my colleagues in the Cardiff Division, and indeed on behalf of my colleagues in Wales, offer you a welcome on your visit to the Principality? We are most pleased to have you with us, and sincerely hope that you will find satisfaction and pleasure in the scientific and social programme which has been arranged.

I would like also to express appreciation of the loyalty of my colleagues in preparation for this meeting, and to thank them and many lay friends and institutions for their co-operation and help. In particular, I would thank the Lord Mayor and Corporation of Cardiff, the President, Principal, and Council of the University College of South Wales and Monmouthshire, and the President and Council of the National Museum of Wales for the use of their magnificent buildings in Cathays Park for the purposes of this meeting.

The British Medical Association was founded in 1832, and this is its 121st Annual Meeting, and it is the fifth time the Association has met in Wales. The first occasion was in 1853, 100 years ago, when the Association met in Swansea. The second occasion was in Cardiff in 1885. The third was a historic meeting in Swansea, 50 years ago, when the Association first met under its new constitution, and the first meeting of the Representative Body took place. The fourth meeting in Wales was held in Cardiff in 1928.

The year 1953 has been regarded as one in which Wales had a special claim to be chosen as the meeting-place of the Association, and we in Wales are pleased and honoured that this has been brought about. It has been a particularly happy coincidence that, on the first day of our meeting, our Royal Patron, Her Majesty the Queen, visited Cardiff as part of her Coronation Tour.

Foundation of the Association

Prior to 1856 the British Medical Association was known as the Provincial Medical and Surgical Association. It was on July 19, 1832, 121 years ago to this month, that at a meeting of over 50 practitioners held in the board-room of Worcester Infirmary it was decided to form a "Provincial Medical and Surgical Association." This decision was taken after an eloquent address from Dr. Charles Hastings, the founder of the Association.

Charles Hastings was then 38 years of age. He was born in Ludlow, and after a period of apprenticeship and having attended private schools of anatomy, but possessing no medical diploma, he succeeded by 134 votes to 133 in obtaining a post of house-surgeon in Worcester at the age of 18. Later he graduated in medicine in Edinburgh, and then returned to Worcester as physician until his retirement in 1862, having been knighted in 1850.

The training of a doctor 121 years ago was very largely by apprenticeship. There remained a few private schools that taught anatomy, physiology, medicine, and surgery, but they were isolated and not associated with hospitals. There was no hard-and-fast line demarcating the qualified from the unqualified practitioner, and this was the case until the Medical Act of 1858.

The year 1832 saw the passing of the first Reform Bill, and during it the Anatomy Act became law. That year also saw the first epidemic of Asiatic cholera in Great Britain, and the medical profession found itself quite unprepared for it.

It was under these conditions that Hastings strove successfully to lay the foundations of an Association which was destined to play so great a part in raising the status of medicine and medical knowledge and practice. In 1828 he established a quarterly journal called the *Midland Medical and Surgical Reporter and Topographical and Statistical Journal*, which continued until the establishment of the Association in 1832.

In the last published volume of this journal there is an account of Hastings's farewell address. He stated that there was a wish that the members of the profession in the provinces should unite into an Association—friendly and scientific—and that it should have as its main object the diffusion and increase of medical knowledge in every department of science and practice, and he earnestly entreated them to join "*with head, and heart, and hand*" in the support of so excellent an Association.

I have chosen the title of this address from the words of Hastings's farewell speech, which was at the same time an inaugural speech in the foundation of our Association. It was indeed not "hail and farewell" but "farewell and hail." The nature of the invitation shows the earnestness of the appeal and a desire to promote that "love of the work" which has been responsible for so much effort of a spontaneous and voluntary nature in medicine. His objective was the increase of medical knowledge, and the foundation of work on a scientific basis and in the spirit of general friendliness. He appealed for support "with head, and heart, and hand," and in these most memorable words Hastings made clear to the profession the attitude to be cultivated for the common good.

One must remember that in those days (1832) the railways had not been developed. Travel was tedious and postage expensive. Conditions therefore were not altogether easy for the convening of meetings and for the diffusion of knowledge, although Hastings well realized how important it was that these difficulties should be overcome. We find that very clearly indicated in the original prospectus, in which the objects of the Association are defined.

The first object was for the collection of information. In those days accurate information was not readily forthcoming to the practitioner, and it was realized that for the advancement of medical science it was necessary to collect information from all sources in order subsequently to convey it.

Another important objective of the Association was to correlate the incidence of epidemic and endemic disease with such varying factors as the nature of the soil, the climate, and the locality, and with habits or occupations. In this objective can be seen the early signs of interest in what are now well-established and important specialties in medicine, such as public health, preventive medicine, and occupational health, which are of prime importance for the welfare of the community.

By no means the least of the objects was that defined as being for the maintenance of the honour of the profession, by friendly intercourse and the promotion of harmony and good feeling. This can surely be regarded as of the greatest importance not only for the profession itself but for the comfort of mind and sense of trust which our patients must have if they are to place their medical care in our hands. The patient can derive full benefit only when he knows that his doctor is trained to attain that high sense of honour and reliability which will in its turn bring to the patient a calm and trusting confidence, with relief of avoidable anxiety.

These intentions of the Association founded 121 years ago, and following a tradition dating back to the time of Hippocrates, have been carried forward continuously ever since.

The Seventeenth, Eighteenth, and Early Nineteenth Centuries

Medical knowledge in 1832 had made considerable progress following the work of the previous two centuries. The seventeenth century brought advances in anatomy and the demonstration by William Harvey of the circulation of the blood. The science of microscopy was developed and applied to disease, and red blood cells were observed. Thomas Sydenham named and described many diseases, was a strong advocate of fresh air in sick-rooms, and produced a therapeutic book which was used by English practitioners for more than a century. A Welsh physician, Charles Clermont, in 1672 published a book on "the airs, waters, and places of England" in which he outlined the medical topography of the country. There was in 1665 that terrible experience when some 70,000 persons died in the Great Plague of London.

With the eighteenth century came advances in physics and chemistry. Carbon dioxide, hydrogen, nitrogen, and oxygen were discovered, and an explanation was forthcoming of the processes concerned in respiration. Electricity began to be applied in the treatment of disease. The obstetrician began to replace the midwife, although operative gynaecology had no real existence. It was the age of William Hunter, anatomist and a leader in obstetrics, whose work and teaching were a source of inspiration. With him was his brother, John Hunter, who laid the foundations of surgical pathology. William Heberden helped to banish many undesirable concoctions from the pharmacopoeia, and Edward Jenner, encouraged by John Hunter, established inoculation against smallpox.

In the early nineteenth century Broussais drew attention to the importance of a diseased organ as a cause of fever. Laennec invented a stethoscope, and the principles of examination of the chest by auscultation and percussion were developed. Richard Bright described nephritis, and differentiated between cardiac and renal dropsy. James Parkinson described paralysis agitans, and in 1812 reported in English, for the first time, a case of appendicitis. The foundations of a school of thought for psychiatry were laid at this time, and Thomas Hodgkin described the disease that was subsequently called by his name. The laryngoscope, the ophthalmoscope, and even the clinical thermometer had not been invented, and there was no hypodermic syringe. Body-snatching for dissection, which had been rife, was checked by the Anatomy Act of 1832.

The dangers of infection and the absence of adequate anaesthesia restricted the bounds of surgery, and there were no general operations on the abdomen and cranium. Those were days before ether and chloroform. Surgery had to be rapid, and the patient's distress was only inadequately relieved by such traditional soporific potions and inhalations as were available.

Medicine therefore in 1832 had reached a stage where knowledge was accumulating, interesting problems lay ahead in profusion, baffling difficulties obstructed adequate treatment, when Hastings and others with him decided on the formation of the Association which they anticipated would materially help the furtherance of medical science.

1832 to 1853

The first 21 years of the life of the Association takes us to 1853, when it met for the first time in Wales. Medical science during this time had again advanced. Purkinje in 1839 introduced the microtome, which enabled tissue to be sectioned suitably for examination with the microscope. He was a physiologist of eminence, and was responsible for introducing the word "protoplasm" into medical language. Oliver Wendell Holmes made some astute observations on the contagiousness of puerperal fever and advocated changing clothes and scrubbing the hands in a solution of calcium chloride. It was on a suggestion by Holmes that the word "anaesthesia" was brought into use. Ether was being used as an anaesthetic in this country in 1846, and Simpson in 1847 introduced chloroform as an anaesthetic for use in obstetrics. In 1848 Robert James Graves, of Dublin, introduced the timing of the pulse by a watch, and described exophthalmic goitre in detail. Thomas Addison in 1849, and subsequently, described the suprarenal glands and their function, and inaugurated the study of the ductless glands, which has since led to so much beneficial research.

It was in 1846 that the first *Medical Directory* appeared, and it was established that unqualified practitioners were about twice as many as those who were qualified.

In the first 21 years the membership of the Association had grown from 310 to 1,853 in the year 1853. An index of the enthusiasm of the Association in those early days is the fact that in Bristol, in 1833, 250 members attended out of a total membership of 316. During this period Branches were formed in various parts of the country, including one in North Wales (1848) and one in South Wales, called the Monmouthshire Branch (1852). It was not, however, until 1871 that the present South Wales and Monmouthshire Branch was formed. It was on August 10 and 11, 1853, that the Association met at Swansea, and considerable developments were to take place before they next met in Swansea in 1903.

1853 to 1903

It was in this period that Darwin stimulated anatomical research by his theory of evolution and great advances were made in experimental physiology, cellular pathology, and bacteriology. Two important diagnostic instruments were invented, the ophthalmoscope in 1851 and the laryngoscope in 1855, following which various other instruments used for endoscopy were in time designed. Lister in 1867 laid before the profession the principles of antisepsis, and introduced catgut into surgical technique. Koch in 1876 demonstrated the bacillus that caused anthrax, and six years later discovered the tubercle bacillus and introduced treatment with tuberculin. Louis Pasteur developed a treatment for hydrophobia with which he was successful in curing a patient in 1885.

The clinical thermometer came into use during this period, and shortly before 1900 there came the discovery of *x* rays by Roentgen, the isolation of radium, the first recorded uniting of a divided artery in man, the first artificial pneumothorax, and the discovery of an agglutination test in the diagnosis of typhoid fever.

Among the many names of those who contributed to the advance of surgery are those of Paget, Hutchinson, Macewen, Treves, Spencer Wells (gynaecologist), and Victor Horsley, who was a pioneer in neurological surgery.

The work of Florence Nightingale in the Crimean War of 1854 and after her return to England gave a new conception of what nursing could be and should be, and led to the development of a nursing service of which we are all proud, and which has contributed so greatly to the advance of medicine and surgery throughout the years.

In this period the death of Sir Charles Hastings took place, in 1866, after serving the Association which he founded for 33 years as Chairman of Council and of which he had been President in 1849. He spent his life in the furtherance of medical science and the honour of the profession.

It was in 1856 that the Provincial Medical and Surgical Association changed its name to "The British Medical Association." This was in keeping with the broadening interest and sphere of work and influence which were developing. Before the end of the century many overseas Branches had been formed, including Jamaica (the first overseas Branch) and various parts of the Empire as far away as Australia, New Zealand, and South Africa.

The Association had always been interested in medical education and high standards of professional work, and by its efforts was largely responsible for the formation of a General Council of Medical Education with the passing of the Medical Act of 1858. One of the functions of this Council was to establish a *Medical Register*, and to authorize the practice of medicine legally. The leading part played by the Association in these matters had its influence throughout the Empire in establishing high standards in medicine, with corresponding uplifting of the profession and improvement in the services rendered to the public.

In 1873, at the Annual Meeting in London, Mr. Gladstone, then Prime Minister, spoke of the Association in the following words: "I believe this Society to be generally representative of the medical profession in its various branches. I believe it represents your tendency to unity and your upward aspirations—upward aspirations not in the sense of augmenting your well-earned and hardly earned emoluments, but in augmenting your unity, augmenting your knowledge, augmenting your true dignity and your claims upon society."

It was about the year 1900 that reforms within the Association were advocated, so that it might be better constituted to undertake the responsibilities ahead. In this stage of reconstruction we remember with gratitude the name of Dr. Alfred Cox, and with him those two other pioneers in this connexion, Victor Horsley and Smith Whitaker. New Articles of Association were drafted and came into force in 1902. They provided "that the primary unit of the Association should be such that every member thereof shall have a reasonable opportunity of attending every important meeting"; that the primary units be called Divisions, and that groups of units constitute Branches. It was also provided that there should be appointed by these units representatives who would be called together as a meeting of representatives to decide the policy of the Association.

Thus was established a body representative of all the members of the Association, for the management of their affairs, and individual members were enabled to participate in the formulation of the Association policy. The first meeting of the Representative Body took place at Swansea in July, 1903, 50 years ago, under the Chairmanship of Mr. (later Sir) Victor Horsley, and the constitution of the Association has carried on ever since.

The Twentieth Century

At the beginning of the twentieth century the doctor worked as an individual and had to rely to a large extent on his stethoscope, a detailed history of the case, a careful physical examination, and his own clinical judgment. Although he employed to the utmost the medical skill of his day, his patients had to bear the full brunt of many diseases, such as pneumonia.

Now half a century has passed by, and with it has gone the hopeless outlook formerly associated with so many diseases. This half-century has seen brilliant and co-ordinated work by individuals and by teams of workers,

medical men and scientists, directed to the cure of disease. The empirical remedies of 1900 have largely given way to the rational and curative remedies of to-day.

We have seen the accumulation of knowledge on vitamins and hormones—e.g., insulin and cortisone. Principles of immunization dating back to Jenner and Pasteur have been applied to diphtheria, tetanus, typhoid, and other diseases. Valuable drugs of sedation, the barbiturates, followed on the discovery in 1903 of barbitone. A great teacher and physician, Sir William Osler, died in 1919. He was responsible for the phrase, "A man is as old as his arteries," and inculcated the principle of "work for work's sake." The painstaking researches of Sir Thomas Lewis on the heart brought the standards of science to the bedside. His work on the skin led to an understanding of the principles of allergy, with its manifold effects on the body.

This has been the age of chemotherapy, beginning in 1903 with the discovery of trypan red, and of antibiotics following the discovery of penicillin by Fleming in 1929. Powerful chemotherapeutic and antibiotic substances are now in common use by the doctor, and have been of enormous help to him in curing his patients of infections. Progress in this field has been rapid and continuous. The scope and possibilities of treatment are ever extending, and these advances are of the greatest importance to the community. These potent remedies, however, have increased the responsibilities of the prescribing physician. They demand considerable care for their safe administration and to ensure that their effect in the relief of symptoms shall not confuse an important diagnosis.

Surgery also has made great advances, and not the least of these has been the improved conditions in the operating theatre. At the turn of the century visitors to the theatre did not wear gowns, gloves and face-masks were not generally used, and the surgeon's gown was clean but not sterile. The emphasis was on antisepsis rather than asepsis. Moynihan played a great part in raising the standard of abdominal surgery. Pioneers in surgery have been abundant, men such as Bland-Sutton, Sargent, Stiles, Grey Turner in this country, and Cushing, Murphy, the Mayos in America.

This era has also seen the development of surgical specialties which inevitably followed the wealth of knowledge which was accumulating, and which had to be directed in concentrated form for special purposes. In Wales we are pleased to remember the part taken by such men as Lynn Thomas, William Sheen, Paterson, H. O. Thomas, Robert Jones, John Williams, and Thomas Lewis in the advancement of our knowledge, as well as many names associated with the development of thoracic surgery. The refinements of radiology, the growth of radiotherapy, and especially the developments in anaesthesia and the routine of blood transfusion, all contributed to the advancement of surgery and in particular the surgery of the thorax and the brain.

Gynaecology has advanced steadily since Spencer Wells in 1858 performed his first operation of ovariotomy. In obstetrics, puerperal sepsis has come under control, and the importance of prenatal care has been appreciated and has received local authority and Governmental support.

Paediatrics also has become an established and valuable branch of medicine, and great advances have been made in our knowledge of other special branches of medicine. There has been continual progress in the field of preventive medicine and public health, and in the control and treatment of infectious diseases.

The study of cancer has been intensively pursued in this country and in various other countries, and great progress has been made in its treatment by surgical and other methods. Nevertheless cancer remains a problem to be solved, and with its complete understanding, which in time will surely come, a great forward stride will have been made.

Research implies effort, deliberate and purposive, and should be given every encouragement and help. The benefits of research are cumulative, and present-day investigation has its foundation on the work of generations past. One discovery tends to breed another, and in this age of discovery the answers to many of our problems may not be so far away.

Ophthalmology

Descriptions of eye diseases and remedies for the eyes have been found dating as far back as 1550 B.C. Some form of operation for cataract was possibly practised in the second century A.D., and Arabian medicine between the tenth and the thirteenth centuries A.D. produced writings on the principles of optics and books on ophthalmology. It was, however, in the eighteenth century, just over 200 years ago, that Daviel, oculist to Louis XV, developed with success an operation for the extraction of cataract, the true nature of cataract having been discovered early in that century. Thomas Young had written on colour vision and on the mechanism of the eye, and was later referred to as the father of physiological optics.

The first public hospital to be devoted to diseases of the eye was Moorfields Eye Hospital in London, which was founded in 1805 and has ever since remained a centre of ophthalmological learning. Eye hospitals began to develop in America some 12 years later, but in France ophthalmology for a long time remained united to general surgery. It was in 1829 that Louis Braille established the Braille system for reading by the blind, which has proved such a boon to those so afflicted. Liverpool founded in 1791 the first Institute for the Blind, followed by Edinburgh two years later. Ophthalmology made great advances following the discovery of the ophthalmoscope by the physiologist von Helmholtz in 1851.

A school of ophthalmology was founded in Vienna in 1854 by Albrecht von Graefe, and an eye clinic was started at Utrecht by F. C. Donders. Von Graefe was a great force in the development of ophthalmology. He established iridectomy for glaucoma, recognized the association of papilloedema with cerebral tumours, established sympathetic ophthalmia as a clinical entity, and with Donders founded *Archiv für Ophthalmologie*. He died of tuberculosis at the age of 42.

In the last half of the nineteenth century ophthalmology developed rapidly, and with the establishment of cocaine as a local analgesic in 1884, in addition to general anaesthesia, operations on the eye became more common, wider in their application, and more successful.

The Ophthalmological Society of the United Kingdom was founded in 1880, and elected for its first president William Bowman, who did so much to elucidate the minute anatomy of the eye and to increase ophthalmological knowledge.

Jonathan Hutchinson, Hughlings Jackson, Argyll Robertson, Swanzy, Nettleship, Marcus Gunn, and Treacher Collins are some of the notable names in this period of rapid development. Progress has continued unabated in the twentieth century. The outlook for cases of detachment of the retina was completely altered in 1929 by the work of Gonin. Traquair, of Edinburgh, by painstaking and magnificent work on perimetry added a diagnostic aid of especial value in neurology. Nobel prizeman Allvar Gullstrand, of Upsala, by establishing the principles of the slit-lamp in 1911, opened up a new field of investigation and a new science of biomicroscopy as applied to the eye. The surgery of cataract and of glaucoma has been developed and improved, and now surgical operations on the cornea have become an accepted procedure and in general use.

We have seen the development and practical application of contact glasses, which can be worn directly on the eye, and the innovation of introducing an acrylic lens into the eye to replace a cataract. A high standard of perfection has been attained in the making of ordinary spectacle lenses, including the development in the last 15 years of the use of transparent plastic material for their manufacture.

Our knowledge of the influence of heredity on diseases of the eye has grown, and it has been shown that congenital malformations may sometimes be attributable to virus infection. The part played by focal infections in producing

diseases of the eye has also received considerable attention, and more recently the investigations of Alan Woods and others have demonstrated how profoundly inflammatory conditions of the eye may be influenced by ocular allergy and varying conditions of general susceptibility or immunity.

Advances in general therapeutic measures have been and are being applied to the eye, and in turn ophthalmology is rendering growing aid to general medicine. Vigorous research is going on, and gaps in our knowledge are being filled, and some firmly rooted views have been shown to be untenable. Textbooks of international fame in ophthalmology have originated in this country, and are in current use.

The intimate processes of life within a cell are now being investigated with the aid of the electron microscope, and radioactive elements are being used in the investigation of normal and abnormal processes taking place in the living body. Biophysics and biochemistry now form the basis for highly specialized research which is opening up new pathways of knowledge.

Ophthalmology indeed has not been lacking, and has shared with its sister specialties the enormous advance that has in recent years become so evident.

Progress, and Association Responsibilities

During the last 50 years, as a result of medical advances, social development, and public health measures, expectation of life in this country has increased by about 18 years. About half the children of to-day should reach the age of 70. Disease is being controlled and many diseases formerly mortal or severely disabling are now being cured.

The British Medical Association has been prominent during the great development and expansion of knowledge of this century, and has taken an active part in the consideration of the events leading up to the establishment of the National Health Service in 1948. The expression of responsible medical opinion on matters which are related to the health of the community or the welfare of the sick always merits the most careful consideration, and the profession willingly devotes its time and energy to such matters, be they of local or of national interest.

Through two world wars the Association was entrusted with the responsibility of mobilizing the profession both for military and for civilian purposes, and is constantly tendering its considered advice to various Government departments. It has applied itself to problems relating to special diseases or groups of diseases, general practice and specialized practice, hospital work, medical education, and medical ethics. Its Divisions and Branches provide widespread opportunities for clinical papers and discussion. It has extended its influence throughout the Empire, and takes a leading part in affairs of world medicine.

One of the great responsibilities of the Association is the regular production of the *British Medical Journal*. The origin of the *Journal* was the establishment of the *Provincial Medical and Surgical Journal* in October, 1840. In January, 1853, the name was changed to the *Association Medical Journal*, and it was on January 3, 1857, that it took on its present name, the *British Medical Journal*.

A copy of the *Journal* is sent weekly to every member, and it has been of the greatest importance in maintaining and expanding the Association. The *Supplement* is a regular feature designed partly in order to keep members informed on the general affairs of the Association and medico-political matters. It was instituted early in 1903.

In 1892 the *Journal* started an epitome of current literature, which endeavoured to summarize some of the more important developments in medicine in various parts of the world; this has now expanded into a separate publication, *Abstracts of World Medicine*. The Association is also now responsible for the publication of fourteen specialist periodicals, and since March, 1951, for that of *Family Doctor*, a monthly health magazine intended for the non-medical reader.

In the field of ophthalmology, the *British Journal of Ophthalmology* is now published by the Association, as well as that most valuable publication *Ophthalmic Literature* in which are abstracts and reviews of current ophthalmological articles, monographs, and textbooks.

Regarding Medical Literature

It has been an inevitable accompaniment of medical progress that there has been a great increase in publication of medical literature. It is not possible to ascertain exactly how many medical periodicals are published throughout the world. If, however, a count is made of those better-known journals which are of value in medicine generally, it appears that, whereas in 1912 there were about 1,654, that number has increased in the last 40 years to nearly 4,000. Many of these appear weekly, others monthly or quarterly. In addition very many books are published. It is quite obvious that no one could possibly attempt to read all these publications even if he confined himself entirely to one specialty and devoted his whole time to the task.

It has therefore been of the greatest importance that this onerous task of reading should have been relegated to teams of workers whose task is to condense, extract, and emphasize important matters and new developments in research. A very full share of responsibility for this type of research has been undertaken by the Association, through its abstracting service, and the organization is now on an international level.

Despite all attempts to condense and epitomize knowledge, it is still very difficult to try to keep abreast of modern knowledge, even in one of the many specialized fields of medicine. New facts come to light constantly, and theories become outmoded and are replaced by new concepts. The general practitioner in medicine has indeed an enormous task to keep himself well informed. Though it is true that he cannot be expected to be familiar with details of specialized knowledge, it is important that he should be familiar with the possibilities of the application of such knowledge for the benefit of his patients. He has to be competent in the diagnosis and treatment of disease, and be himself able to prescribe discriminately and treat very many maladies in patients who rely solely on him for their medical care. Old remedies have to be supplanted by new. Traditional treatment may have to give way to more effective modern therapy.

In order to attain proficiency the doctor has to read. Reading takes time, and time in medicine is often a scarce commodity. It is, in the end, bad for medicine, and consequently bad for patients, that a doctor's routine work should so absorb his time as to leave little or no opportunity to read. There seems justification for emphasizing the need for leisure time in every medical man's life both to enable him to read and to allow some respite from the trying life which he normally leads.

The *British Medical Journal* provides a medium for dissemination of knowledge. It is read by specialists and general practitioners alike, and from its inception has been a valuable broad guide to the advances of the past. The difficulties of presenting in brief form the practical lessons of world research are enormous. It is, however, in just that way that a journal such as ours can be of so much benefit to so many by epitomizing current thought and directing attention to important developments, as well as by recording original work. It was Osler who once said, "A new era has come in medicine . . . the world has become a single country."

Medicine has never been regarded as narrow and confined, but has extended to the limits of human endeavour without regard to race or creed. The practice of medicine is our duty, our honour, and our privilege, and we are proud to remember the words of Hastings, the founder of our Association, who entreated us to serve "with head, and heart, and hand."

FAMILIAL IDIOPATHIC METHAEMOGLOBINAEMIA

ASSOCIATED WITH MENTAL DEFICIENCY AND NEUROLOGICAL ABNORMALITIES

BY

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The idiopathic form of methaemoglobinaemia is a rare condition, and Finch (1948) found only 16 examples recorded in the literature. All cases had been cyanosed from birth or from an early age. Litarczek *et al.* (1930), Miller (1930), and Dieckmann (1932) described the manifestations of the disorder and emphasized its differentiation from the toxic form of methaemoglobinaemia, which may result from such substances as bismuth subnitrate, aniline and its derivatives, acetanilide, sulphonamide preparations, nitrophenol, and various nitrites, including drinking-water contaminated by nitrates, which are converted into nitrites in the intestine (Ewing and Mayon-White, 1951).

A familial incidence has been reported by several observers, including Baltzan and Sugarman (1950) (15 cases in a family-tree extending over four generations); Barcroft *et al.* (1949) (seven cases in two families); Bensley *et al.* (1938) (brother and sister); Breakey *et al.* (1951) (brother and sister); Codounis *et al.* (1947) (14 cases in a family of several generations); Deeny *et al.* (1943) (two brothers); Hitzenberger (1942) (three brothers); Lian *et al.* (1939) (a mother and five children —three brothers and two sisters); and Lutembacher (1949) (six cases in four generations).

Codounis *et al.* (1947) as well as Baltzan and Sugarman (1950) considered that familial methaemoglobinaemia was inherited as a Mendelian dominant. The evidence from earlier records, however, indicated that the inheritance was of a recessive character, a view supported by the more recent report of Breakey *et al.* (1951).

The outstanding clinical feature of idiopathic methaemoglobinaemia is that of cyanosis of lavender hue, especially of the lips, cheeks, nose, and buccal mucosa, dating from birth or very early life, remaining constant apart from treatment, and persisting throughout life. The general condition is usually good; the heart and blood vessels are normal and most patients do not complain of symptoms. In some examples, however, headache, vertigo, muscular cramps, asthenia, tachycardia, and mild dyspnoea have been described; such symptoms have been attributed to an insufficiency of blood oxygenation. Mild polycythaemia (5,500,000 to 6,000,000 red corpuscles per c.mm.) with increase in the mean corpuscular diameter, and slight leucocytosis, polymorphs predominating, have also been recorded (Lian *et al.*, 1939).

Expectation of life is apparently normal, and cases are mentioned at 70, 75, and 80 years of age.

The three siblings we describe with idiopathic methaemoglobinaemia were all mentally defective and each had the same type of strabismus. They also showed abnormalities of the tendon reflexes; in two of the cases both the knee- and ankle-jerks were absent as well as the deep reflexes of both arms; in the third case one ankle-jerk and all arm reflexes were absent. Abnormalities of the tendon reflexes do not appear to have been recorded in association with methaemoglobinaemia, and mental deficiency is very unusual, only Hitzenberger's case being mentally defective as well as physically undersized, and van den Berg's (1905) patient being described as "a not very intelligent man."

Two of the children were observed to be "blue" at birth, and cyanosis was first noticed in the other child at the age of three months.

Case 1

A girl aged 8 years and 10 months was first seen in December, 1948. She is the second child of the family. Her elder sister, aged 11, is free from cyanosis, is of normal intelligence, and is in good health. The patient was blue when born; the labour had been normal. The infant sucked poorly and moved very little; her mother stated that "she lay like a doll in the pram." She did not walk until she was 3 years old, nor did she make any attempt to speak until about the same age.

On examination the child showed generalized cyanosis, especially of the cheeks, lips, ears, roof of mouth, and hands, together with the brownish tinge of the skin characteristic of methaemoglobinaemia. She had an internal concomitant strabismus; apart from scanty retinal pigment the fundi were normal. Her speech was an almost unintelligible drawl. All four limbs showed normal movement and power. The radial, supinator, biceps, and triceps jerks were all absent; both knee- and ankle-jerks were also absent. The plantar responses were equivocal and the abdominal reflexes were very sluggish but equal. Co-ordination was normal. The heart and other systems were normal; the pulse rate was 80; and blood pressure 115/75. Intelligence tests showed that the child's mental age was only 3 years with an I.Q. of 34, indicating middle-grade imbecility. She could count numbers only up to 3, had no idea of letters, and no drawing capacity. Her speech was mainly a babble, with a few clear words and phrases emerging as at a 2-years level. In manipulation she was very awkward and had great difficulty in using a pencil.

Investigations.—*X*-ray examination of the chest showed no abnormality; electrocardiograms were normal. Cerebrospinal fluid was normal, with negative Wassermann and Lange reactions. Blood count: red cells, 5,250,000; packed cell volume, 46%; reticulocytes, 1.7%; total pigment 84%; colour index 0.8; white cells, 8,400 (polymorphs 65%, lymphocytes 25%, monocytes 4%, eosinophils 5%, basophils 1%); W.R. negative.

Methaemoglobin was estimated with a hand-spectroscope. On December 30, 26% of the total blood pigment consisted of methaemoglobin. An intravenous injection of 7 ml. of a 1% solution of methylene blue was given that day; within half an hour of the injection the cyanosis had disappeared, the child was looking pink and healthy, and investigation revealed no methaemoglobin in the blood. For the next 12 days the child was given 200 mg. of ascorbic acid twice daily by mouth; nevertheless, four days after starting the ascorbic acid she was again cyanosed and the blood methaemoglobin had risen, but to a lower level than before the injection of methylene blue—11% as compared with 26%. After 12 days ascorbic acid was discontinued and the percentage of blood methaemoglobin gradually rose, to reach 20% in nine days. Ascorbic acid (400 mg.

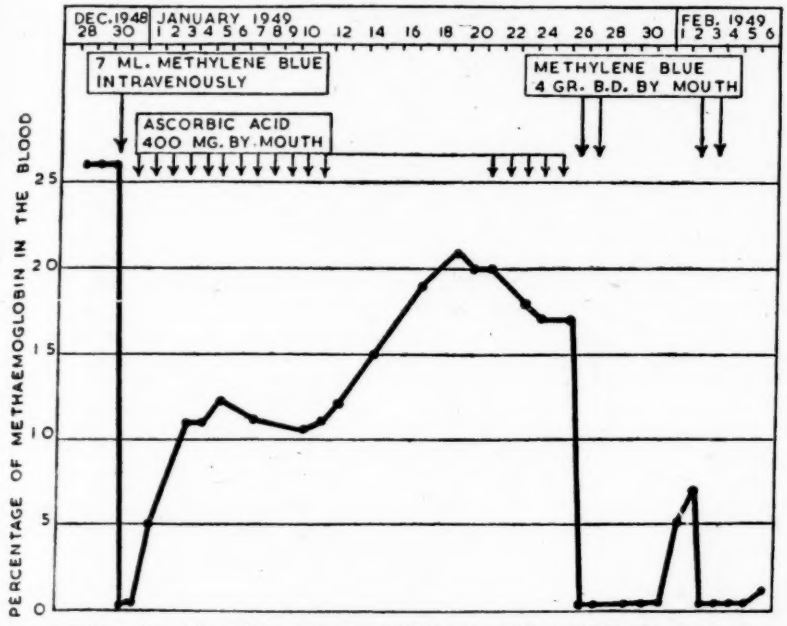

DEC. 1948
28 30
JANUARY 1949
1 2 3 4 5 6 7 8 9 10 12 14 16 18 20 22 24 26 28 30
FEB. 1949
1 2 3 4 5 6
7 ML. METHYLENE BLUE INTRAVENOUSLY
ASCORBIC ACID 400 MG. BY MOUTH
METHYLENE BLUE 4 GR. B.D. BY MOUTH
PERCENTAGE OF METHAEMOGLOBIN IN THE BLOOD
0
5
10
15
20
25

FIG. 1.—Case 1. Idiopathic methaemoglobinaemia. Effect of injecting 7 ml. of a 1% solution of methylene blue intravenously, and of giving ascorbic acid and methylene blue by mouth.

daily) was then resumed and the blood methaemoglobin gradually fell to 17% in five days. Next, 4 gr. (0.26 g.) of methylene blue in tablet form was given twice daily by mouth for two days. Within an hour of the first dose the cyanosis had disappeared, and for five days there was only a faint trace of methaemoglobin in the blood; on the following day it had risen to 5% and next day to 7%. A further dose of 4 gr. (0.26 g.) of methylene blue again caused the methaemoglobin to disappear from the blood (see Fig. 1).

Case 2

A boy aged 7, and next in the family to Case 1, was first seen on February 24, 1949. He is said to have been normal at birth, but was noticed to be "blue" at the age of 3 months; the cyanosis has persisted. He did not sit up until 12 months old, and did not walk or talk until the age of 3½ years.

On examination the child showed the same generalized cyanosis as his sister, especially of the cheeks, lips, and buccal mucosa. He also had an internal strabismus. The pupils and fundi were normal. Speech was confined to a few simple words. All deep reflexes in both arms were absent, but the knee-jerks were present and equal; the right ankle-jerk was absent and the left sluggish. Both plantar reflexes were flexor. Co-ordination was very poor.

Intelligence tests showed his mental age to be 3 years and 10 months, giving an I.Q. of 47. His vocabulary was very limited and approximated to that of a child of 3 to 4 years, but most of his speech was intelligible. He could count up to 12 and was fairly good at space and form relations in recognition tests, but at less than a 4-years level.

Investigations.—*X*-ray examination of chest, and the electrocardiogram, revealed nothing abnormal. Cerebrospinal fluid was normal, with negative Wassermann and Lange reactions. Blood count: red cells, 5,560,000; packed cell volume, 45%; reticulocytes, 1.8%; total pigments, 86%; colour index, 0.78; white cells, 10,000 (polymorphs 71.5%, lymphocytes 22%, monocytes 5.5%, eosinophils 0.5%); W.R. negative.

Investigation of the blood daily for eleven days showed that the amount of methaemoglobin varied from 12 to 18% of the total blood pigment. At 11.30 a.m. on March 7 he was given 4 gr. (0.26 g.) of methylene blue by the mouth; by 12.15 p.m. his cyanosis was replaced by a healthy pink colour: at 12.30 a sample of blood showed no trace of methaemoglobin. Three further doses of 4 gr. (0.26 g.) of methylene blue were given at 12-hour intervals. No methaemoglobin was detected in his blood until March 10, when a slight trace was found; on the 11th there was 6%, and it had risen to 16% by the 14th. He was then given 4 gr. (0.26 g.) of methylene blue twice daily by mouth for two days, which again abolished the cyanosis and reduced methaemoglobin in the blood to nil; by March 21, however, it had risen to 8% (see Fig. 2). Subsequently it was ascertained that 4 gr. (0.26 g.) of methylene blue by mouth twice a day for two days kept him free from clinical cyanosis and from detectable methaemoglobin in the blood for about five days.

Case 3

A younger brother of Cases 1 and 2, aged 3 years and 5 months, was first seen in March, 1949. He was "blue" at birth and labour had been normal. His progress has been very slow and he has always been backward; he sat up at 10 months and has not yet spoken.

On examination the child showed about the same degree and distribution of cyanosis as his sister and brother, and also an internal strabismus. He was only just beginning to walk on a widened base. Co-ordination both of arms and of legs was very poor, although showing a full range of movement. The knee- and ankle-jerks, as well as all deep reflexes in the arms, were absent. The plantar reflexes were flexor and the abdominal reflexes present and equal. The heart showed a faint apical systolic murmur, but the other systems were normal.

On attempting intelligence tests (Dr. Ruth Griffiths) it was necessary to resort to tests for an infant of 6 months. His development age was approximately 9 months, with a developmental quotient of 20. The child had no speech, could stand alone for only a short period, and walked on

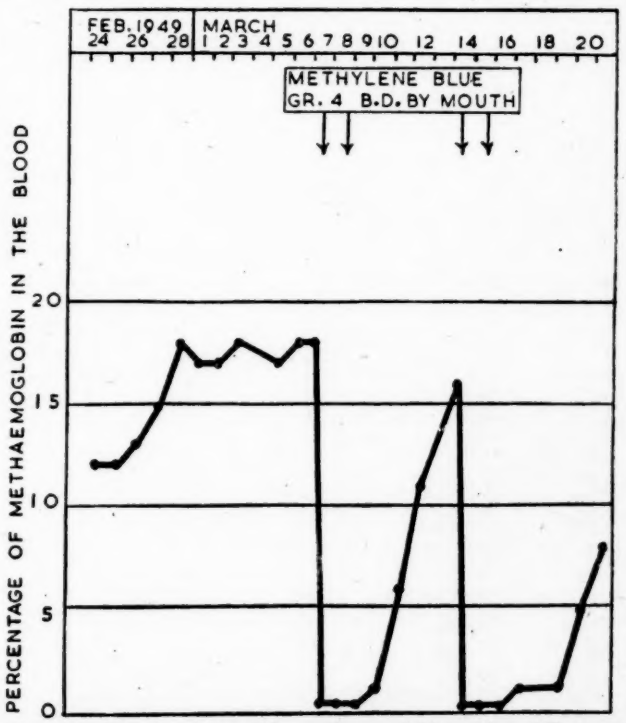


FIG. 2.—Case 2. Idiopathic methaemoglobinaemia. Effect of giving methylene blue, 4 gr. (0.26 g.) twice daily for two days by mouth.

a widened base when led. He was not very interested in materials, and his manipulative skill was poor. He was unable to feed himself, and had not acquired control of his excretory functions.

Investigations.—*X*-ray examination of the chest was normal. The cerebrospinal fluid was normal with negative Wassermann and Lange reactions. Blood count: red cells, 5,050,000 per c.mm.; packed cell volume, 38%, reticulocytes, 1%; total pigments 76%; colour index, 0.75; white cells, 4,400 (polymorphs 38%, lymphocytes 51%, monocytes 5%, eosinophils 6%).

Estimation of the blood over a period of one week showed the methaemoglobin to average 20% of the total blood pigments. The child was put on methylene blue, 2 gr. (0.13 g.) twice daily, on April 10 for two consecutive days. As with his sister and elder brother, after the first dose the cyanosis disappeared and no methaemoglobin could be detected in the blood (see Fig. 3). Without further methylene blue, the blood methaemoglobin had returned to its former level of 20% by April 21. By taking 2 gr. (0.13 g.) of methylene blue twice daily for two consecutive days of each week he remained relatively free from cyanosis.

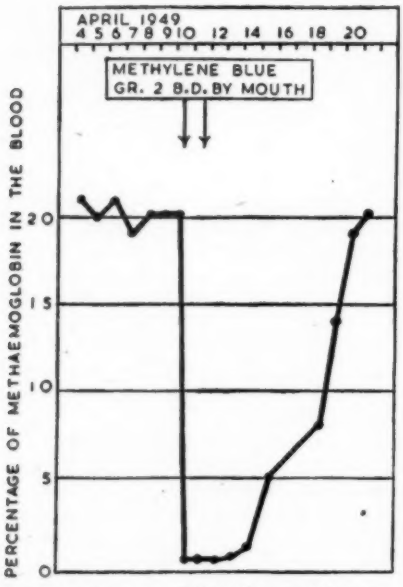


FIG. 3.—Case 3. Idiopathic methaemoglobinaemia. Effect of giving methylene blue, 2 gr. (0.13 g.) twice daily for two days by mouth.

Observations on the Cases

Cases 1 and 3 showed some eosinophilia. Examination of the faeces on several occasions, including specimens after an enema, showed no worms, ova, or cysts.

The methylene blue in each case was given in the form of plain tablets each of 2 gr. (0.13 g.). Sugar-coated tablets of methylene blue were tried, but these appeared relatively inert as regards effect both on the cyanosis and on the blood methaemoglobin, the coating of the tablets probably interfering with absorption.

After some months Case 3 refused to take methylene blue tablets. Consequently, he was put on the following:

Methylene blue	1 gr. (65 mg.)
Syrup of tolu	10 min. (0.6 ml.)
Chloroform water	to ½ oz. (14 ml.)

One tablespoonful twice daily on three consecutive days of each week.

Although the reduced amount of methylene blue did not abolish the cyanosis, this was rendered less apparent, with considerably reduced blood methaemoglobin.

The morphological haematology of the three affected children's blood was essentially normal. Mean corpuscular volumes were normal, and the mean corpuscular concentrations of total pigment, measured as alkaline haematin, were 30–31%. Reticulocyte percentages in all three fluctuated from less than 0.1 to 2.4%, but the observations were spread over periods with and without treatment. The aspirated marrows were not significantly different from normal. The overall picture did not therefore suggest any acceleration of formation and destruction of erythrocytes.

The methaemoglobin in the blood was entirely intracorpuscular, and the plasma was also free from methaemalbumin and was not icteric. The blood of the mother and of the eldest child was normal, and methaemoglobin was not detected with the Hartridge reversion spectroscope.

The excretion of coproporphyrin was measured in Cases 1 and 2, but the daily average was only of the order of 15 μg. in the urine and 50 μg. in the faeces (White and Ventura, 1951). These figures are well below those reported by Dobriner *et al.* (1937) for a normal 12-year-old child. Brownlee (1939) and Rimington and Hemmings (1939) found that increased coproporphyrin III excretion occurs in the methaemoglobinaemia due to various aromatic compounds and sulphonamides, and suggested an increased rate of breakdown of the methaemoglobin through paths leading to porphyrin formation. This does not appear to be so in the present cases, although the possibility of imbalance between excretion of coproporphyrins I and III was not investigated.

The effect of ascorbic acid and methylene blue therapy on the haemoglobin and methaemoglobin content of the venous blood of Cases 1 and 2 was examined on a number of occasions. The principal results are given in Fig. 4. The methods and reference frame are those adopted by King *et al.* (1951). On the Haldane scale 100% = 14.8 g. of Hb per 100 ml.; using the Huffner factors, the iron content is 0.34%, and 1 g. Hb = 1.34 ml. of O_2 or CO. The total pigment findings agree well when determined by iron content, as alkaline haematin or cyanhaematin, or by carbon monoxide capacity after reduction, but the oxygen capacity decreases in proportion to the amount of methaemoglobin present.

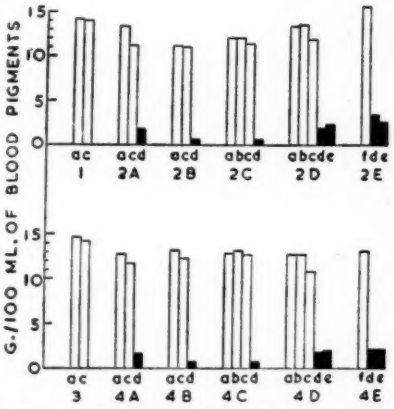


FIG. 4.—Blood pigments of normal and affected members of the family. 1.—*Mother's blood.* Methaemoglobin absent. 2.—*Case 1.* 2A: Blood after six weeks without treatment. 2B: Five days later, after 300 mg. of ascorbic acid a day. 2C: Blood taken after one month of treatment by methylene blue, 4 gr. (0.26 g.) twice daily on two days a week. 2D: Eighteen days later, no methylene blue being given during this time. 2E: Ditto, 22 days from 2C. 3.—*Blood of normal eldest child* (girl aged 11). Methaemoglobin absent. 4.—*Case 2.* 4A–E: Conditions as for 2A–E.
a: Total blood pigment in grammes per 100 ml., estimated by iron content. b: Ditto, estimated by CO capacity after reduction. c: Ditto, estimated by oxygen capacity. d: Grammes of methaemoglobin per 100 ml. of blood, estimated in Klett spectro-colorimeter. e: Ditto, estimated in the photo-electric colorimeter. f: Total pigment by alkaline haematin.

Grateful acknowledgment is made to Dr. R. J. Bartholomew and Miss M. Geiser for their co-operation in these observations, and to Mr. A. H. Latham.

The methaemoglobin was directly measured as a percentage of the total blood pigment by use of the Klett spectro-colorimeter (King *et al.*, 1947). It was also measured photocolorimetrically; the decrease in absorption at 630 μ on conversion of the methaemoglobin to cyanmethaemoglobin was compared with the absorption when all the pigment dilution of the sample was converted to methaemoglobin with ferricyanide (King and White, 1949, unpublished observations).

In-vitro experiments on the reduction of methaemoglobin were carried out with cells from Cases 1 and 2, and from a further case of idiopathic methaemoglobinaemia (Dresner, Tay, and White, 1951, unpublished observations), and are summarized in Tables I, II, and III. Ascorbic acid may have a relatively great effect *in vivo*, despite the limited concentrations which can be reached in the plasma, by lessening the gap between the rates of production and reduction of

TABLE I.—*In-vitro Experiment on the Reduction of Methaemoglobin in the Red Cells from Cases 1 and 2 by Ascorbic Acid and Methylene Blue*

Case No.	Total Pigment Concentration in g./100 ml. and Millimols*	Unincubated Cells	Methaemoglobin as % of Total Pigment Cells Incubated for 2 hours at 37° C. in Isotonic Sodium Chloride with:		
			No addition (Control)	2·5 mg./100 ml. Ascorbic Acid (0·14 mM)	0·25 mg./100 ml. Methylene Blue (0·0067 mM)
1	7·8 g. 1·14 mM	19	11·1	12·8	6·1
2	6·5 g. 0·96 mM	16·6	14·8	12·0	5·4

* Mol. Wt. of Hb, 68,000.

TABLE II.—*Further Experiment on the Reduction of Methaemoglobin in the Red Cells of Case 1 by Increasing Concentrations of Ascorbic Acid*

Total Pigment Concentration in g./100 ml and Millimols	Methaemoglobin as % of Total Pigment				
	Unincubated Cells	Cells Incubated for 2 hours at 37° C. in Isotonic Phosphate Buffer with:			
		No addition (Control)	50 mg./100 ml. (2·8 mM) Ascorbic Acid	500 mg./100 ml. (29 mM) Ascorbic Acid	2·5 g./100 ml. (0·144 mM) Ascorbic Acid
7·8 g 1·14 mM	115	14	11·3	5	Haemolysis and destruction of haemoglobin

TABLE III.—*In-vitro Experiments on the Reduction of Methaemoglobin in the Red Cells of a Further Case of Idiopathic Methaemoglobinaemia (female, aged 21) by Anaerobic Incubation with Ascorbic Acid and by Methylene Blue. Administration of 300 mg. of Ascorbic Acid Daily by Mouth Subsequently Reduced the Methaemoglobin from 26% to 7% of the Total Blood Pigment in Seven Days*

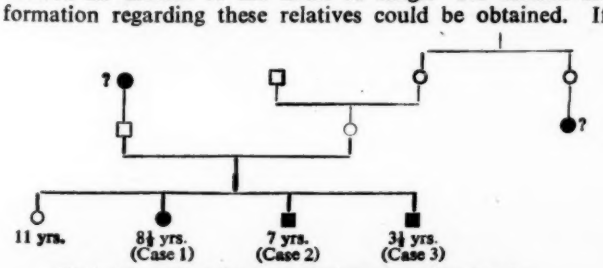
Total Pigment Concentration in g./100 ml. and Millimols	Methaemoglobin as % of Total Pigment						
	Unincubated Cells	Cells Incubated for 12 hours at 37° C. in Isotonic Sodium Chloride with:					
		No addition (Control)	5 mg./100 ml. Ascorbic Acid (0·28 mM)	50 mg./100 ml. Ascorbic Acid (2·8 mM)	100 mg./100 ml. Ascorbic Acid (5·6 mM)	Methylene Blue added. 0·27 mg./100 ml. (0·0073 mM)	
						Anaerobic	Aerobic
11·3 g. 1·67 mM	29	26	15·4	9·2	3·5	18·5	12

methaemoglobin. *In vitro*, however, it is not as active as methylene blue; Barcroft *et al.* (1945) often found slow and incomplete reduction, but with increased activity when the ascorbic acid was protected under anaerobic conditions.

Discussion

In none of these three cases was there any history of diarrhoea, drug-taking, or haemolysis.

Their mother stated than one of her female cousins had blue cheeks "like the children." The paternal grandfather was invalided from the Army during the 1914–18 war on account of "blueness," although it was stated that he showed no disease of the heart or lungs. No further information regarding these relatives could be obtained. If these vague histories, however, can be accepted as evidence of methaemoglobinaemia, we may construct a family tree as shown at the foot of the previous column.



Black circle = affected females; Black square = affected males.

The oxidative change from haemoglobin to methaemoglobin, and the reverse, take place readily in plasma until a point of equilibrium is reached. In the intact red blood corpuscle, however, an enzyme system reconverts the methaemoglobin as rapidly as it is formed, and under normal conditions there is never more than 1 or 2% in the cell. Idiopathic methaemoglobinaemia is an inborn error of metabolism probably due to a congenital defect of a component of this enzyme system—co-enzyme factor 1 (Gibson, 1948; Eder *et al.*, 1949), so that haemoglobin is largely converted into methaemoglobin, and the concentrations of the two pigments are nearly equal in amount. This occurs also in those cases of methaemoglobinaemia with haemolysis—for example, blackwater fever. In poisoning with substances such as acetanilide and dinitrotoluene, methaemoglobin is formed too rapidly for the cell enzyme system to cope with its reconversion. Methylene blue facilitates the reconversion of methaemoglobin, not by direct chemical reaction with the pigments, but by accelerating the normal enzyme process in the red blood cell (Finch, 1948).

It is tempting to regard persistent anoxia as the cause of the mental deficiency and areflexia in our cases, but it is more probable that both the methaemoglobinaemia and the mental defect are inherited separately, possibly as recessive characters from heterozygous parents (Penrose, 1950). In Huntington's chorea, for instance, the dementia and the chorea are transmitted by separate genes. As stated previously, only two other cases of the association of mental deficiency with methaemoglobinaemia appear to have been reported—those of Hitzenberger and van den Berg. Consequently, the coincidence of mental deficiency, abnormalities of the tendon reflexes and methaemoglobinaemia in our three cases in one family is a striking one. A point in favour of the argument that anoxia is the cause of the mental deficiency in these cases is the high percentage of low-grade defectives in one family in this particular social stratum. The common finding is that when mental deficiency occurs in a professional-class family one of the children is a low-grade defective and the others of average or above-average intelligence; but if mental deficiency appears in a lower-class family all the children tend to be high-grade defectives, with an I.Q. of about 75.

As regards the possible association of mental deficiency with other inborn errors of metabolism—in the porphyrias, for instance—we have not encountered mental deficiency, nor are we aware of any reports of such an association. Mania may supervene during the attacks of "acute" porphyria, but it seems to be secondary to the metabolic condition and is not constant. On the other hand, in the rare condition of phenylketonuric or phenylpyruvic amentia (Penrose, 1935; Folling *et al.*, 1945) the metabolic disorder is definitely associated with mental deficiency and is inherited as a Mendelian recessive character.

The symptoms in all reported cases are surprisingly mild considering the degree of anoxia present. For instance, one of the two brothers examined by Deeny *et al.* was able to play a strenuous game of hockey. The three children we describe were no exceptions. Although there was usually a deepening of the cyanosis on crying or on undue exertion, they did not appear to be handicapped so far as their physical condition was concerned. The mildness of symptoms is probably to be explained by the chronicity of the condition. The mild compensatory polycythaemia which was present in all of our patients, as stated previously, is usual.

Lian *et al.* (1939) demonstrated the beneficial action of ascorbic acid in methaemoglobinaemia both *in vivo* and *in vitro*, an observation subsequently confirmed by Deeny *et al.* (1943), Sievers and Ryon (1945), and King *et al.* (1947). Lian and his co-workers showed that, *in vitro*, using a laked blood containing 39% methaemoglobin, 0.05 g. of ascorbic

acid caused the abnormal pigment to disappear in six hours, but it reappeared after 24 hours. *In vivo*, 0.1 g. of ascorbic acid, taken over a period of three weeks, reduced a 45% methaemoglobinaemia to one of 25% ; after six days without ascorbic acid, however, the methaemoglobin in the blood was found to have reached its former level.

Hartmann *et al.* (1938) and Cox and Wendel (1942) obtained beneficial results with methylene blue in the treatment of methaemoglobinaemia caused by sulphonamides, while Schwartz and Rector (1940), Sievers and Ryon (1945), and King *et al.* (1947) demonstrated its value in reducing the blood methaemoglobin, and consequently the cyanosis, in cases of idiopathic methaemoglobinaemia.

Lian and his co-workers considered that the effect of ascorbic acid was superior to that of methylene blue in diminishing the methaemoglobinaemia, while King *et al.* (1947) regarded both substances as effective. In our Case 1, however, methylene blue was more effective than large doses of ascorbic acid in diminishing the percentage of blood methaemoglobin (Fig. 1) and reducing the cyanosis. It was for this reason that Cases 2 and 3 were treated solely with methylene blue. Nevertheless, the improvement in our patients was only temporary, and in order to maintain the beneficial effect it was necessary to repeat the dosage of methylene blue each week. Except for the rapidity of the changes in the cyanosis and the blood methaemoglobin level, administration by the mouth was quite as satisfactory as by the intravenous route. In any case, repetition of intravenous injections would be impracticable in a restless child and difficult to arrange under home conditions. No toxic effects from the methylene blue were seen over a period of two and a half years' observation, thus confirming the opinion of King *et al.* (1947) that methylene blue can be continued to be given orally without ill effect. The only drawback is that, in hospital, the nursing staff dislike the bright-blue stains on the bed-sheets from the urine of ill-controlled bladders.

Over a period of two and a half years' observation the three children described have remained free from noteworthy cyanosis provided they take the methylene blue on two days of each week. In the case of the two elder children, the dosage is 4 gr. (0.26 g.) twice daily for two days and in the younger child 2 gr. (0.13 g.) on each of the two days of treatment. No demonstrable improvement has occurred in the mental condition of any one of the three children, each showing approximately the same I.Q. as formerly. The state of the tendon reflexes, however, has improved to a slight extent in Cases 1 and 2. In Case 1, who originally showed total areflexia, a very slight left knee-jerk and right ankle-jerk can now be obtained on reinforcement ; the other tendon reflexes are still absent. Case 2 shows supinator jerks, but they are unequal, the left being brisker than the right, and also a sluggish right ankle-jerk, previously absent. All tendon reflexes are still absent in Case 3.

Summary

The cases of three siblings suffering from familial idiopathic methaemoglobinaemia are described.

In each of the three children, the inborn error of metabolism was associated with mental deficiency and abnormalities of the tendon reflexes, two of the children showing total areflexia.

Records of other familial examples are mentioned and the literature of the condition briefly reviewed.

Large doses of ascorbic acid (400 mg. daily) were found to be efficacious in reducing the percentage of methaemoglobin in the blood and consequently the cyanosis, confirming the results of other observers. Methylene blue, both intravenously and by the mouth, was found to be even more efficacious, and was continued on two days a week without ill effect over a period of more than two years' observation.

No beneficial effect on the mental condition of the children was noted as a result of treatment, but slight improvement (reappearance) in some of the tendon reflexes occurred in the two elder children.

Acknowledgments are due to Dr. L. Osler, Dr. W. Leese, and Mr. Charles Wyatt for their considerable help in the investigations, and to Dr. P. H. R. Anderson, Divisional Medical Officer, Surrey County Council, for drawing our attention to the cases.

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THE NATURE OF TIC DOULOUREUX

TREATMENT BY ALCOHOL BLOCK OR SECTION OF THE GREAT AURICULAR NERVE

BY

R. WYBURN-MASON, M.D., M.R.C.P.

It was shown by Weddell (1940–1) that each unit area of the skin is innervated by multiple fibres which approach from different directions and weave themselves into a complicated network surrounding hair shafts and bulbs, and sebaceous and sweat glands. Moreover, there is a great deal of overlapping of the spinal-nerve-root supply of any given area of skin or of deep tissues. There is no reason to suppose that the trigeminal area differs from other zonal areas in this respect or that there should not be an overlap of the sensory supply of the area from neighbouring spinal nerve roots.

The Cervical Plexus and the Trigeminal Area

The anterior primary divisions of the second and third cervical nerve roots divide into two, and the adjacent parts of each root join to form the great auricular, lesser occipital, and cutaneous cervical nerves beneath the sterno-mastoid muscles. The latter appear at the mid-point of the posterior border of the muscle, where they pierce the deep fascia, usually immediately above and behind the external jugular vein, which crosses the posterior border of the muscle at the same point. The great auricular nerve then ascends towards the lobe of the ear, crossing the muscle obliquely, and, as it does so, divides into anterior and posterior branches (see Fig. 1). The posterior branch joins the posterior auricular branch of the facial nerve behind the ear, communicates with the lesser occipital nerve and the auricular branch of the vagus, and supplies the skin over the mastoid process. The anterior branch unites with the various branches of the facial nerve as they lie on and within the substance of the parotid gland. Other branches supply the lobe of the ear, part of the posterior and lower portion of the auricle, the skin over the angle of the jaw, and the parotid gland. The great auricular nerve is purely sensory, and some of its fibres join the facial nerve and with it pass to all parts of the face. It appears, therefore, that sensory fibres from the cervical plexus are carried into the trigeminal area with the facial nerve.

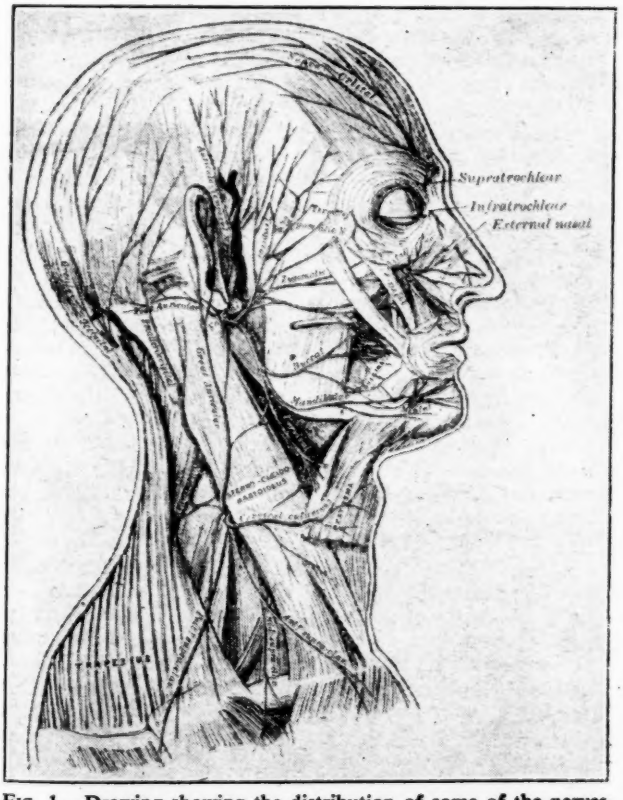

FIG. 1.—Drawing showing the distribution of some of the nerves of the cervical plexus (from *Gray's Anatomy*, reproduced by courtesy of Longmans, Green and Co.). The communications of the great auricular and cutaneous cervical nerves with the branches of the facial nerve are to be seen.

The cutaneous cervical nerve crosses the neck transversely forward from the mid-point of the sternomastoid muscle and its branches supply the skin of the upper and anterior part of the neck passing on to the face. Branches from the cervical branch of the facial nerve join with it. A communication from the cervical plexus (C 1 root) joins the hypoglossal nerve and with it passes into the tongue, to which it supplies sensory fibres and in which it communicates with the lingual nerve. The cervical plexus, of course, innervates all the muscles of the neck, including the sternomastoid and trapezius, with both motor and sensory fibres. The trigeminal nerve supplies pain fibres to the trigeminal area and these enter the medulla from the nerve root and pass caudally in the descending tract of the nerve to end against the nucleus of this tract lying in the first and second cervical segments of the cord. Hence, all pain impulses in the head and neck eventually pass into the upper four cervical segments, and anatomically the sensory nerves of the cervical plexus also partly innervate the trigeminal area.

In some subjects the external jugular vein crosses the posterior border of the sternomastoid muscle well below its mid-point, and it cannot be used as a surface marking for the great auricular nerve. The course of the nerve can then only be marked on the surface by mensuration as described in most anatomy books. In such cases the surface marking is in my experience often far from accurate.

After the trigeminal ganglion has been injected with alcohol some degree of analgesia develops in the trigeminal distribution. This is assumed by most to be complete, but some degree of cephalic sensation remains, especially for pain (Harris, 1937; Mettler, 1948). Carmichael and Woollard (1933), in their earlier experiments, found deep pain sensibility still present in the cheek in such subjects, but a modification of their technique suggested this was not so. They found that procaine blocking of the facial nerve at the stylomastoid foramen caused facial palsy, but no alteration in deep pain sensibility over the face. At this site, of course, the communicating fibres from the great auricular and lesser occipital nerves have not yet joined the facial nerve. An occasional experience of those who have carried out a large number of trigeminal alcohol injections or root section is that successful production of apparently complete trigeminal analgesia has failed to relieve the pain of facial neuralgia or that "ghost"-like twitchings continue, though they are not painful. In other cases root section or injection of the trigeminal ganglion with alcohol results in trigeminal analgesia, but the spasmodic facial pain is replaced by a severe deep constant aching, which may involve not only the trigeminal area but also the whole side of the face and head.

Tinel (1930) described a significant case of left facial neuralgia in which, eight months after successful alcohol injection of the ganglion, the subject was injured in a railway accident and then developed head pains of a different character and distribution from the facial neuralgia. They radiated over the whole left face, jaws, scalp, occiput, and upper neck, and were burning in nature like causalgia, but there also existed paroxysmal crises, produced by eating, swallowing, and especially by emotion, and accompanied by marked flushing of the left half of the face and head. Examination showed that analgesia still appeared complete in the trigeminal distribution, but deep pain sensibility was found to be present over the face and, in fact, was much increased (hyperalgesia), though sweating was abolished over the trigeminal area. In such cases of persistent dull pain following trigeminal nerve section Carmichael and Woollard also found that blocking of the facial nerve at the stylomastoid foramen with procaine caused facial palsy, but had no effect on the pain. At this site, it must be repeated, the communicating fibres from the great auricular and lesser occipital nerves have not joined the facial nerve.

Procedure for Alcohol Block and Surgical Section of the Great Auricular Nerve

Alcohol block of the great auricular nerve can be carried out, as the nerve lies on the surface of the sternomastoid muscle, which prevents the alcohol from affecting other important structures. The patient lies on his side with the head in line with the body. The point where the external jugular vein crosses the posterior border of the muscle is determined by digital compression of the vein at the root of the neck. This makes the vein stand out. A line is drawn on the skin from this point to the lobe of the ear, and about ½–1 in. (1.3–2.5 cm.) along it the skin is anaesthetized with 2% procaine just to either side of the line. Through the skin a size 20 needle is passed down to the level of the deep fascia and 0.5 ml. of absolute alcohol is injected gradually, while withdrawing the needle and pointing in different directions, but taking care to keep it on the surface of the muscle and not to inject into the skin itself. The same procedure is carried out in the second area of anaesthetized skin.

When the alcohol enters the nerve it causes intense burning pain in the region of the ear and just behind it, in the temple, pre-auricular region, forehead, and sometimes in the eye. This lasts about thirty seconds, and the lobe of the ear usually looks red and hot. Within a short while—a matter of a minute or so—the lobe of the ear may feel slightly numb and may appear pale. For several days after the injection there may be some slight local ache in the region of the injection. In some cases it is impossible to find the nerve because of the obesity of the patient, because the external jugular vein takes an abnormal course, or because of some other anatomical variation. The test for whether the nerve has been entered by the alcohol is the development of the typical distribution of pain. Afterwards the lobe of the ear and the skin of the neck below it feel slightly numb to the touch.

The nerve may be sectioned surgically by making an incision transversely to the upper part of the sternomastoid muscle and dissecting down to the fascia covering the muscle, at the same time avoiding the external jugular vein lying anterior to the nerve. The branches of the nerve are then identified and cut, and as much as possible of the nerve is removed. The effect of this is to cause slight numbness of the lobe of the ear and of the skin of the neck below.

If the alcohol is injected only on the surface of the sternomastoid muscle it does not cause any damage to important neighbouring structures. The injection is very much simpler and less painful than that of alcohol block of the trigeminal nerve or ganglion, and also entails less risk of damage to important structures. I have seen few complications from the injection, except that on several occasions the alcohol did not block, but only irritated the nerve. In some of these cases painful labial herpes developed on that side. The pain, however, passed off in a few days. The disadvantage of alcohol injection, of course, is that it is not permanent and that it causes local fibrosis, which may render identification of the nerve at operation difficult. The operation of surgical section of the nerve is, of course, simple and far less formidable than that of craniotomy and section of the trigeminal nerve root with its attendant risks. The only complications have been slight local infection of the wound on some occasions; but this has always rapidly cleared up. Unlike trigeminal block or section, there is no danger of neuroparalytic keratitis, nor any uncomfortable analgesia from either alcohol injection or section of the great auricular nerve. From anatomical considerations and the radiation of pain on alcohol injection of the nerve it is obvious that the great auricular nerve must partly innervate the trigeminal area.

Some Significant Observations on Tic Douloureux

Tic douloureux, or facial neuralgia, is always attributed to disturbance in the pain fibres of the trigeminal nerve, but there are certain observations which do not fit such a concept. Thus:

1. Tic douloureux does not result from pressure or irritation of the trigeminal ganglion or nerve root, which instead causes a dull boring pain accompanied by "trophic" changes in the skin and deep tissues in the trigeminal area. Electrical stimulation of the root at operation also does not give rise to painful tic.

2. No constant lesion has ever been demonstrated in the trigeminal nerve fibres or nerve roots in cases of tic douloureux.

3. While the pain is often found in the area innervated by the trigeminal nerve, it commonly extends beyond this (Harris, 1926). The cases are then termed "atypical." They are in all other respects identical with those in which the pain occurs only within the trigeminal area. In these "atypical" cases the tic may be felt behind the ear, in the distribution of the posterior auricular branch of the facial nerve, which receives branches from the great auricular nerve; below the angle of the jaw, in the distribution of the cervical branch of the facial nerve, which joins the cutaneous cervical nerve; or even in the occiput, in the distribution of the great occipital nerve, a branch of the cervical plexus.

4. Spasms of painful facial tic are often accompanied by flickering or twitching of the facial muscles or may be associated with facial palsy or spasm (Harris, 1926), hence the name tic given to it. When the tongue is affected by pain it may twitch. Cushing (1920) described a condition, which he called "painful tic convulsif," in which violent pain in the eye and face was accompanied by unilateral facial spasm. This was unrelieved by removal of the trigeminal ganglion, but stopped when the facial nerve was cut. Such observations suggest that the pain is mediated by fibres in the facial nerve.

5. Any movement of the facial, tongue, or neck muscles may precipitate the tic. The facial muscles receive afferent fibres by way of the great auricular nerve, the tongue muscles from the cervical plexus by way of the hypoglossal nerve, and the neck muscles by the cervical plexus, suggesting that the impulses giving rise to pain may originate in the fibres of the plexus.

6. I observed a patient who had had a left hemiglossectomy for carcinoma of the tongue carried out three years previously. Three months prior to examination he noticed a lump in the left side of his neck about the mid-point of the sternomastoid muscle, and this was followed by severe aching in the frontal, temporal, and occipital regions of the head and the side of the neck reaching to the shoulder.

He also developed sharp stabs of typical painful facial tic affecting the face and frontal and temporal regions of the head. These were brought on by eating, sleeping, moving the head, or by touching the left side of the face. During examination it was found that pressure on the lump in the neck, which was involving the great auricular nerve, would induce typical neuralgic pains in the face. Alcohol block of the nerve was carried out and the pain was completely relieved over the next four months.

7. I had under observation another patient who developed left-sided herpes of C 2 and C 3 zonal distributions. After three to four weeks he complained of stabs of pain in this side of the face, affecting the cheek, eye, forehead, and tongue, and identical in character with that of painful facial tic.

8. Another patient suffering from Hodgkin's disease received *x*-irradiation over the cervical plexus for enlarged lymph nodes. This, of course, results in irritation of the nerve fibres, including the great auricular, in the irradiated area. At the height of the reaction the patient developed typical painful tic and later facial palsy, which gradually cleared up with the inflammatory reaction to irradiation.

9. Bues (1952) reported a case of carcinoma of the parotid gland involving the facial nerve with marked tic douloureux and disturbance of sensation in the lobe of the ear, indicating a lesion of the great auricular nerve. The nervous symptoms were relieved by radiotherapy to the tumour.

10. In all cases (about 56) of tic douloureux examined by me in the past five years it was found that pressure over the great auricular nerve may either start off an attack of painful tic or cause it to cease if one was present. If the nerve was now blocked with procaine, the facial tic was relieved while the analgesic was acting, though if pain involved the tongue such a procedure did not relieve the pain in this distribution.

11. Harris (1926) described a case of thrombosis of the posterior inferior cerebellar artery with complete analgesia and thermo-anaesthesia over the trigeminal area, in which pains developed like those of tic douloureux in the analgesic area. He also mentions three cases of fracture of the base of the skull involving the trigeminal nerve and producing complete trigeminal motor and sensory paralysis. In these, pains like those of tic douloureux occurred in the analgesic area. It seems difficult to incriminate the trigeminal nerve as the pain pathway in such cases.

12. While alcohol injection into the trigeminal nerve or root section may abolish the pain of tic douloureux, in some cases after a short while the pain returns undiminished. In others, ghost-like flickerings like those producing pain persist in the previously painful area, but are unaccompanied by pain. These are precipitated by the same factors as the original pain. I have found that if the great auricular nerve is now blocked with procaine or alcohol the analgesia in the trigeminal area becomes both more profound and more extensive and the pains may cease as in the following case.

Case 1

A man aged 62 years was first examined in January, 1943. For the previous 18 months he had suffered from severe sharp stabbing pain in the left forehead, the side of the nose, and the cheek, especially in the angle of the mouth, spreading to behind the ear. The tongue and gums were not affected. Pain was induced by speaking, eating, touching the face, and turning the head, and was accompanied by flushing and twitching of that side of the face. Injection of the trigeminal ganglion with 1 ml. of absolute alcohol was undertaken and resulted in complete loss of superficial sensation over the trigeminal distribution, with relief of pain for about six months. During this time, however, there was a good deal of tingling and a swollen sensation in the face, and he noticed sudden shootings in the region where pain had previously been experienced, but these did not give rise to pain, though they were identical in other respects with the sensations present with the pain.

At the end of six months these shootings again became painful, and eventually the pain returned as severely as before. Although analgesia seemed still complete, trigeminal alcohol injection was undertaken again with relief of pain as before, though the paraesthesiae and occasional dartings persisted. About two years later, during cold weather, he had a slight return of the painful tic, which recurred at intervals, especially when he was emotionally upset, in cold weather, and when he had a cold. He also developed persistent trophic sores in the left temporal region of the scalp, in the external auditory meatus, and by the side of the nostril, and frequent attacks of blockage and running from that side of the nose, often accompanied by sneezing, left-sided tinnitus, catarrh, and deafness.

When examined in October, 1948, superficial analgesia was still present over the trigeminal area and there was marked tenderness on pressure over the great auricular nerve. It was observed that, if he had a spasm of pain, pressure on the nerve caused it to stop suddenly, though this was followed after some minutes by increased paraesthesiae on the side of the nose and lips. The great auricular nerve was infiltrated with 2 ml. of 2% procaine, which caused the pain and paraesthesiae to cease immediately. The injection of the absolute alcohol induced burning over the analgesic area for a few minutes, but from that time the paraesthesiae and pain ceased, the trophic sores except in the temporal region healed within a week, and the blockage and running from the left nostril cleared up. When seen two months later the trophic sore in the temporal region was still present. The left lesser occipital nerve was therefore blocked with alcohol. When the patient was seen again one month later this sore had also healed. At the same time the analgesia of the scalp had extended backwards for some 2 in. (5 cm.) (see Fig. 2).

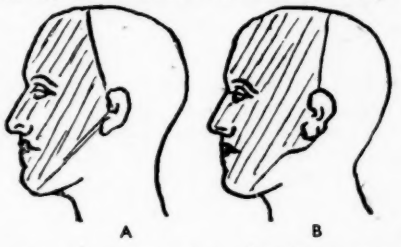

FIG. 2.—Extent of "trigeminal" neuralgia: A, before, and B, after alcohol block of the great auricular and lesser occipital nerves in Case 1.

Such procedures have now been carried out on 14 similar cases. In six of these surgical section of the great auricular nerve was necessary in order to stop the pain, as attempts at alcohol block of the nerve were unsuccessful for various reasons, such as anatomical variations in the course of the external jugular vein, the landmark for the nerve, or obesity of the neck. It appears that, while complete blocking of the trigeminal pathways exists, pain of either aching or paroxysmal character may be present over the trigeminal area and side of the head, and this is abolished by blocking the branches of the cervical plexus.

13. In cases of tic douloureux, if the great auricular nerve is exposed in the neck under local analgesia and its branches are touched with forceps, typical painful spasms can be produced in the face in the area where they occur spontaneously. This has now been carried out on numerous occasions, and was well seen, for example, in the following case.

Case 2

A man aged 49 had had typical painful tic for three years, during which time he had had periods of up to four months free from pain. When first examined the pain affected the right frontal region, eye, cheek, and upper and lower lips. It was precipitated by eating, speaking, moving the head, and by touching a "trigger" zone of skin on the upper lip. The bouts of pain were accompanied by slight twitching of the facial muscles around the eye, flushing of that side of the face, and slight lacrimation. The present attack had lasted some four weeks, during which he had been off work and was now completely demoralized.

Examination.—The patient held his head and neck taut and still, and was apprehensive of being touched, especially on the face. The only other abnormal physical sign was some tenderness on pressure over the right great auricular nerve in the neck, which gave rise to typical spasms of pain. The nerve was injected with alcohol under local analgesia. This caused transient intense pain over the whole of the right side of the face and ear, and as soon as this had died down, even with the needle still in position, the patient was able to rub his face vigorously, speak, smile, and move his head. All spontaneous pain and the facial spasm ceased.

After six months he again began to suffer from typical spasms of pain, which, however, were now restricted to the upper lip,

cheek, and side of the nose. An attempt was made to reinject the great auricular nerve. This, however, proved difficult owing to the local fibrosis, and, while the upper extent of the pain was somewhat diminished, it still persisted in the lower part of the affected area. The great auricular nerve was therefore exposed as it lay on the sternomastoid muscle, and two branches, an anterior and a posterior, were identified. On touching the latter with the forceps no pain was experienced. The posterior branch of the nerve was evidently still interrupted by the previous alcohol injection. When the anterior branch was touched, however, it produced typical pain over the cheek and upper lip of great intensity and identical with that occurring spontaneously. The removal of 1¼ in. (3.8 cm.) of both branches was followed by complete abolition of the painful tic and by slight analgesia of the lobe of the ear and the region of the parotid. The patient has had no recurrence of pain over the last 18 months.

Discussion

I have now treated some 56 cases of tic douloureux either by alcohol block or by surgical section of the great auricular nerve. In all cases alcohol block was attempted first, and in about half was completely successful in relieving the pain, provided the tongue was not involved. However, in the other cases only partial or transient relief was obtained, and surgical section was carried out later. The treatment does not relieve the pain in the tongue. The patients have now been followed up for as long as five years. In cases treated by alcohol block alone the pain may return after 6 to 18 months and reinjection or surgical section has to be carried out. Of the 25 cases in which surgical section was undertaken, two have had some return of pain after intervals of two and a half and three and a half years, respectively.

From the above observations it seems impossible to escape the conclusion that, at least in a proportion of cases, tic douloureux is a disturbance of the great auricular nerve and other branches of the cervical plexus. It seems possible that the pain in the face is mediated through the fibres of the great auricular nerve, and that in the tongue through the fibres of the cervical plexus which join the hypoglossal nerve. Whether this is the basis of symptoms in all cases remains to be seen. If so, then how is it that interruption of the trigeminal nerve may give relief from the pain? It may be that this causes a local atrophy of the nerve networks in the skin and tongue mucosa, which also receive fibres from the great auricular nerve.

Summary

Reasons are adduced for believing that, at least in a proportion of cases, tic douloureux is due to a disturbance of the branches of the cervical plexus, especially of the great auricular nerve and the branch which joins the hypoglossal nerve.

A method is described for alcohol block and surgical section of the great auricular nerve, which has been used in the treatment of tic douloureux involving the face.

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Endrocrinological research in Sweden is to be promoted by a donation of Kr. 1,000,000 (£68,965) from the Knut and Alice Wallenberg Foundation to the Carolinian Institute, Stockholm, the foremost medical research centre in Sweden. New buildings for endocrinological investigations are to be built with the donation. The Wallenberg Foundation was established in 1917.

IN-PATIENT CARE OF GENERAL HOSPITAL PSYCHIATRIC PATIENTS*

EXPERIENCE WITH 500 CASES

BY

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In the accompanying table is given an analysis of 500 consecutive patients seen personally for diagnosis and treatment in the Department of Psychiatry at Leeds University. Apart from the psychosomatic group, which it is proposed to discuss separately, there is little on which to comment in these figures. They have, of course, no universal significance, as they depend on the referring doctors. They merely give an impression of the kind of psychological problem dealt with in one particular setting.

The Patients According to Diagnostic Groups

Psychoneurosis			170(21)
Hysteria		47(10)	
Obsessional-compulsive state		5(2)	
Anxiety state		118(9)	
Depression (mania, 4)			92(12)
Dull and backward			11(1)
Mentally deficient			8
Epilepsy			10(4)
Addiction (chronic alcoholism, 3; ether, 1; thyroid, 1)			5(1)
Cerebral organic states			42(3)
Toxic—exhaustive states	4	Hypertensive deficit	2
Cerebral tumour	7	Parkinsonism	1
Head injury	7	G.P.I.	2
Arteriosclerosis	6	Cerebral syphilitic	1
Senile degeneration	3	Paget's disease	1
Pre-senile states	1	Myoclonus	2
Bromide intoxication	1	Unknown lesions	3
Delirium tremens	1		
Paranoia			3
Schizophrenia (including paraphrenia)			13(2)
Psychopathic personality (including sexual deviation)			43(5)
Psychosomatic conditions (other than psychoneurotic)			79(7)
No psychiatric abnormality found			24(1)

Fifty-seven of these patients (the diagnoses are given in parentheses in the above table) were admitted to psychiatric beds in the General Infirmary at Leeds, being dealt with among general medical patients in the ordinary wards, under conditions no different from those applying to any other type of illness. The following are reasons for admission: (1) For physical examination and investigation. (2) For psychiatric observation, or more detailed psychological examination than was possible as an out-patient. (3) For specific treatment, such as E.C.T., abreaction, stabilization of analeptic therapy, and so forth. (4) To give relief from an acutely dangerous or unfavourable environment. (5) To assist in establishing a psychotherapeutic role on the part of the physician. (6) To allow of continuity of treatment when a patient had been investigated in a medical or surgical bed and it was not possible to keep him there as long as would be desirable for his further psychiatric investigation or treatment. (7) For convenience, because attending from a considerable distance and more than one interview was required.

Admission for Physical Investigation

This is usually a straightforward issue when a patient presents with a symptom which may be connected with a disorder of mechanism. There are a number of subjective complaints which are particularly apt to be misunderstood: common examples include tiredness in anaemia; shoulder

*Adapted from a paper read at the Annual General Meeting of the Northern Branch of the Royal Medico-Psychological Association at the Department of Psychiatry, University of Leeds, in April, 1952.

pain in relation to cervical slipped disk; fatigue in hypertension; pain in a young patient with atypical or doubtful coronary thrombosis; and tachycardia in minimal hyperthyroidism. In many cases investigation may best take place in a routine way elsewhere in the hospital. But admission to a psychiatric bed often carries intangible advantages: initial rapport is maintained, for example, or the psychological perspective is not confused; and sometimes the psychiatrist can conduct the physical investigation quite adequately without further help. General physicians are apt to underestimate the capacity of their patients to follow and understand physical problems under investigation. It is easier to play a reassuring omniscient part than to acknowledge uncertainty about some physical disorder. At any given moment in a psychotherapeutic relationship there is a limit to the amount of information the patient should be given; but, equally, there is a limit to the appropriate medical reserve.

Psychotherapeutic rapport with an intelligent patient quite often requires, or is strengthened by, an admission of fallibility or explicable uncertainty. With minor hypochondriasis a useful technique has been to reassure the patient, explaining the limits of physical examination and investigation, and then to suggest review at some definite and appropriate point ahead, say in three, six, or nine months' time. This clears the air for further psychotherapeutic discussion, and reinvestigation often proves unnecessary.

It is a truism that the psychiatrist should carry out a full physical examination; or should make sure that a patient is, or has been, thoroughly examined physically elsewhere. Further, there is a proper time for this, usually before any formal therapeutic moves; and to conduct a thorough physical examination is part of the routine by which the psychiatrist gives confidence both to himself and to the patient. But at times there seems to be some quality in the psychiatric relationship which militates against intensive physical investigation and treatment, as distinct from a limited physical examination. The difference between the psychiatrist and the general physician seems to be something of this sort—that the psychiatrist is trained to be passive, and permissive; to allow patients to express themselves in their symptoms, or their behaviour; and, in fact, to be tolerant of disability, and, by a special attitude and by special techniques of discussion, to establish a relationship which will help in giving the patient confidence and insight. This applies even with the use of active physical treatment: the permissive, passive, tolerant approach remains a basic part of psychiatric technique.

In modern physical medicine and surgery, on the other hand, the doctor is trained, unavoidably, in a probing, searching, critical attitude, almost aggressive at times in its intensity, with a willingness to intervene in an objective way quite independently of the patient's understanding of the situation. It may be that there is an inevitable conflict here, and that to combine the qualities required for first-class psychiatric care with those demanded by modern physical methods of investigation is an almost impossible achievement, attainable only by a degree of dissociation—a kind of Jekyll and Hyde situation, where who is which will depend on one's brand of clinical practice.

If so it should be a greater stimulus than ever towards bringing the general physician and the psychiatrist into a group relationship. Team work among surgeons is taken for granted. Given mutual experience and understanding of group dynamics, it should be possible for combined physical and psychiatric treatment to be conducted by team-work, rather than through the traditional techniques of individual responsibility. This would require something closer and more purposeful than the loose co-operation which is normally taken for granted in the wards.

Admission for Observation

Usually the evidence about a patient's behaviour comes from three sources: the information from the patient himself, observation during interview, and information from relatives. Sometimes, however, there is a straightforward difficulty in that out-patient interviews may simply not give an opportunity to see enough of the patient. As an example, the following case may be quoted.

An Irish labourer aged 21 was referred to the medical out-patient department because of his bizarre complaints. His accent was so thick that at first we thought he was Polish. It took some time to establish rapport sufficient to elicit his complaints fully. They included attacks of what he called "shivering out"—a phrase which he used as if the doctor must at once know what he meant, and which referred to shivering all over the body lasting a minute or so, and developing at the end of micturition, mostly in the evening. At a later interview he revealed the idea that there was something inside him in the pubic region which was very slowly eating him away. In spite of the odd picture, very much like schizophrenia, there was a reasonably good affective relationship, and the background was satisfactory. He was living in a hostel, and shared interests (cards, dog-racing, and cinema) in a satisfactory way with others, although there was evidence of immaturity, with some odd personality traits. No hallucinations or formal delusions other than his half-understood hypochondriacal one could be found. He was admitted to the ward, his physical state was investigated (with negative results), and his relationship with nurses, occupational therapists, and other patients was observed. His level of intelligence was confirmed as average, and, with increasing response, the emotional problems relating to his simple upbringing in Ireland and his transition to the rather stressful industrial environment of Manchester and Leeds were discussed with him. He then was able to reconsider the unrealistic nature of his ideas about his body. Observation in this case was of great assistance in avoiding premature conclusions which might have had serious results for his freedom of action.

The psychiatric patient should not be left to a routine based on chance administrative arrangements and clinical tradition in other branches of medicine. This is a natural tendency, since all concerned—psychiatrists, nursing staff, and administrators—have been unaccustomed to thinking of patients with emotional illness as a definite group within the general hospital. The psychiatrist, however, can utilize his mental hospital experience, because in this area mental hospital and general medical practice find common ground. When a patient is admitted to a mental hospital he has been, in one sense, introduced to a special kind of group therapy. He passes through various stages of adjustment. After the experience of admission, whether voluntary or compulsory, there comes the process of establishing relationships in one particular ward or unit of the hospital. As time goes on, no matter what specific forms of treatment are administered, he becomes increasingly aware of the therapeutic status of the different wards and treatment groups, and passes from one to the other, making small serial adjustments to the reality of each new environment, until finally he is in that hospital group which is living virtually a normal life, and from which he returns home.

There is a therapeutic advantage in arranging a similar process in the general hospital. It must naturally vary according to personal experience and local circumstances. The system evolved in dealing with the patients quoted here has been along the following lines.

(*a*) *Phase of Admission.*—Preparation of the patient, with explanation and discussion of the purpose behind admission. If resistance is pronounced it may be wise to postpone admission.

(*b*) *Initial Rest in Bed.*—Physical examination and investigation. At the end of this stage, which may be very short or quite prolonged, appropriate psychotherapeutic discussion of physical findings is advisable.

(*c*) *Patient up and About Within the Ward, in a Dressing-gown.*—Occupational therapy has started meanwhile in bed, and the patient, in dressing-gown and slippers, begins now to attend the out-patient department, which in this hospital is on an upper floor. In some cases visiting from outside will have been limited up till now; in others encouraged.

(*d*) *The Patient's Clothes are Brought.*—From now on, therapeutic interviews are held away from the ward, in the psychiatric department, which requires the patient to cross a public street. This provides a natural reason for his being required to dress.

(*e*) Sooner or later the patient is encouraged to stay out of hospital for a short walk or for a cup of coffee, before returning to the ward. On visiting days relatives may take the patient out instead of sitting at the bedside. At all times, however, the patient's movements are subject to the ward sister's agreement, and are expected to fit in with the ward arrangements.

(*f*) Finally, the patient leaves hospital for a spell at an ordinary convalescent home, away from specific psychiatric supervision.

Admission for Specific Treatment

With care and flexibility, practically all the therapeutic psychiatric methods such as psychotherapy, hypnosis, narco-analysis, E.C.T., abreaction, and modified insulin or other drug therapies can be fitted in conveniently to a basic regime of this kind, which gives a sense of progress while allowing for the maintenance of the all-important permissive relationship throughout. Suitability of patients, however, does vary to some extent with hospital facilities. Powers of co-operation by hospital staff have to be carefully assessed. Emotionally disturbed patients tend to act out their feelings with other patients as well as the nursing staff, and the psychiatrist carries the responsibility of judging the resilience and tolerance of these other environmental figures in the group situation, so that discretion demands sometimes that the patient should not stay. Hysterical and psychopathic patients are the chief cause of trouble. Some day further specific training of the general hospital nurse in psychotherapeutic methods may be helpful in this kind of situation. It is striking, however, that at present, almost without exception, sisters and senior nurses show considerable intuitive understanding of difficult patients. Even with the most aggressive or hostile patient it is practically always the young and inexperienced nurse who makes serious errors.

Many authors have discussed the value of E.C.T. for in-patients (Sargant and Slater, 1946; Sands, 1946; Mallinson, 1948), but one is inclined to agree with Neustatter (1951) that E.C.T. in psychoneurotic and psychosomatic patients has surprisingly little place. Many depressed patients of the reactive type, admitted for E.C.T., start improving while initial *x*-ray and other investigations are being done; and very soon it may become contraindicated, as being likely to slow up adjustment rather than hasten it. On the other hand, the early psychotic patient does not show this beneficial reaction to admission on the whole, and E.C.T. in such a case follows in due course. A development which deserves mention in this connexion is the use of short-acting relaxants in association with E.C.T., which now permits of the whole procedure being carried out behind screens in the general ward, without distress to others.

Escape from Environmental Stress

There are two main occasions when environmental stress justifies admission. One is when the patient is displaying symptoms which are a direct reaction to stress, or are manifestly made worse by an unsatisfactory emotional set-up at home. In asthma, for example, symptomatic relief may show almost at once on admission, and patients are sometimes found who over many years had invariably been well in hospital and seriously ill at home. For such, admission to a general hospital may be inappropriate, and a long-stay neurosis centre perhaps may provide a better answer (where such a centre exists). But there are many less-well-defined syndromes in which physical manifestations fluctuate with emotional strain. Although these are to some extent physiological, and although the temporal relationship may at times obscure rather than point the connexion, as when migraine develops after and not during a period of emotional tension, admission alone may be a valuable therapeutic step.

A special case is the patient who turns up as a casualty, sometimes brought in by the police. The history is often confused, incomplete, and contradictory, and the patient may be emotionally cathartic, weeping, and struggling; or stuporous and uncooperative. A psychopathic personality is sometimes recognized only too readily; but the wear and tear of dealing with such a patient at short notice, possibly requiring literally hours of attention in the middle of some complicated programme, is greatly eased by the facility of admission. Social dynamics begin to work, and with the invaluable aid of a psychiatric social worker the whole objective picture may become plain within two or three days. One can then turn to the problems of treatment. Once such a patient knows his way to the casualty department, he tends to return from time to time, but his background is then understood, and further admissions may not be necessary.

The other prominent justification for admission to escape from environmental influences is when the latter are obscuring diagnosis or prognosis. Particularly in patients with reactive depression, a psychoneurotic pattern may become quickly apparent as soon as gross environmental strain is relieved, with a corresponding change in prognosis.

Establishing Psychotherapeutic Rapport; Transfer from Other Beds; Admission from a Distance

The value of admitting a patient for psychotherapy alone is very doubtful, chiefly because to adapt to an environmental problem he should be in day-to-day touch with his difficulties. Even where there is some other reason for admission, such as a bodily illness quite separate from his psychological condition, psychotherapy often proves ineffective. There are only two occasions which occur at all frequently when in-patient psychotherapy in the general hospital may be helpful in its own right: first, when the patient is transferred from the care of a physician or surgeon elsewhere in the hospital; and, secondly, when the distance from home to hospital limits out-patient attendance severely.

The second of these is a straightforward problem of convenience, but the first may be clinically useful. Practically all psychosomatic patients, and many psychoneurotics, pass through the hands of the physician or surgeon in the first place. Often, therefore, the psychiatrist is asked to see such a patient in hospital as part of the general investigation, or at the end of it, when physical findings are complete. No matter how well conducted their investigation, these patients do often have many doubts about themselves and their complaints. To be able to transfer them to a psychiatric bed, and establish the psychotherapeutic relationship before discharge, may then be most useful. The physical investigation can be made to take its natural place, whereas it may otherwise remain at times seriously misunderstood. This, of course, should not happen when a psychosomatic approach has been applied, whether intuitively or as a result of training.

Integration of Mental Hospital and General Hospital Psychiatry

The 500 patients referred to here represent the kind of material found in every general hospital. It does not seem to be known how many psychiatric beds are provided for such patients, but one has the impression that they are too few. In a combined memorandum of the Royal College of Physicians of London, the British Medical Association, and the Royal Medico-Psychological Association in 1945 it was concluded that 5% of beds should be available in those general hospitals where a psychiatric out-patient clinic is held regularly. Blacker (1946) suggested, for a start, the provision of 100 beds outside mental hospitals per million of the population, apart from observation ward accommo-

dation. It was part of his concept that all grades of mental hospital staff should be offered part-time appointments, thus encouraging diverse extramural activities, and that general hospitals and mental hospitals should have staff in common.

Although many general hospital patients may never enter a mental hospital there is certainly no natural clinical cleavage between those who do and those who do not. Experience underlines similarities rather than the opposite, especially in techniques of management. If, then, one envisages a policy of treating as many psychiatric patients as possible in the general hospital, how is it best achieved? Henderson and Gillespie (1950) thought that treatment in the wards of a general hospital should be regarded as a provisional arrangement pending the establishment of specially constructed and equipped psychiatric clinics within general hospitals. Apart from observation wards, whose special function excludes them, the York Clinic stands out in this country as almost the only deliberate attempt at achieving such an aim, with close physical contiguity to other parts of the hospital. Such a unit is essentially what most mental hospitals try to supply in the form of admission wards. But can anything else be attempted? In an address to the Association of Occupational Therapists Lord Webb-Johnson (1951) is reported to have said that one of his own great ambitions was to see all voluntary patients, and all borderline patients, treated in a general hospital. This would be a revolution indeed, and if widely developed it would inevitably mean bringing the present staffs of mental hospitals to work with in-patients in the general hospitals also. Sargant and Slater (1946) are among those who have suggested its clinical practicability. It would also be in line with the ideals of the joint memorandum already quoted.

But is this not really a question which should be explored in a purposeful, experimental way, to supplement evidence which is at present tenuous? For example, would it not be possible to arrange a clear-cut long-term experiment, within the ordinary administrative arrangements of a progressive general hospital, by which beds therein could become the part-time responsibility of a mental hospital consultant, assisted by his staff, and admission to which would be only by transfer from the mental hospital? The mental hospital consultant would, in effect, be given general-hospital facilities for the experiment. We have to discover the answers to two main questions: first, how many patients can be treated successfully in the general hospital who are at present treated successfully in the mental hospital? and, secondly, what special administrative arrangements and regimes would be necessary for this? One has in mind the serial group relationships mentioned earlier, as well as such matters as provision of day-rooms, problems of staffing, and the use of convalescent homes for prolonged rehabilitation. The answers to these two questions cannot safely be assumed, and their investigation could play a powerful part in encouraging further integration of psychological and physical medicine.

I am glad to acknowledge Professor D. R. MacCalman's permission and encouragement in dealing with, and describing, these patients.

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At the annual general meeting of the Royal Institute of Public Health and Hygiene, held in London on July 2, Mr. Walter Elliot, C.H., F.R.S., presented certificates of Honorary Fellowship to Mr. F. J. M. Bengué, founder of the Bengué Memorial Award, and to Mr. H. H. Gerrans, Secretary of the Institute.

SEROLOGICAL FINDINGS IN A CASE OF HAEMOLYTIC ANAEMIA

WITH SOME GENERAL OBSERVATIONS ON THE PATHOGENESIS OF THIS SYNDROME

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The application of new serological methods has made a further classification of the syndrome "haemolytic anaemia" easier. Whereas up to a short time ago a classification into "familial" and "acquired" types (excluding acquired haemolytic anaemia due to known aetiological agents) was possible only by clinical means and family investigations, the discovery that one type of acquired haemolytic anaemia is accompanied by the presence of antibodies in the blood of the patient made it possible to separate this type from the rest.

Antibodies had been postulated already in 1940 by Dameshek and Schwartz as the causative agents of all haemolytic anaemias. Definite proof, however, of their presence in certain types of haemolytic anaemia was obtained only in 1946, when Boorman, Dodd, and Loutit used the Coombs test (anti-human globulin test) for the investigation of their cases. They found that the cells of certain patients suffering from the acute and obviously acquired type of the disease gave a positive Coombs reaction, and interpreted these findings as proof of the presence of antibody globulin on the surface of the cells of these patients. They also reported that the sera of their patients who were found to have a positive Coombs reaction gave no indication of containing an antibody other than a low-titred "cold" agglutinin or "pseudo"-agglutinin. Since then, however, a number of cases have been described in which the presence of antibodies in the serum of the patient could be demonstrated by means of the indirect Coombs test. These antibodies were designated pan-agglutinins, since they acted upon all red cells tested, and on occasion, in consequence, no donor compatible with the patient could be found. Kidd (1949) eluted the antibodies from the red-blood cells of his patients and found them to act on all cells of his panel. He states that "to date, no human red cell has been found which cannot be fully coated or sensitized by exposure to the action of these eluates."

In our experience, previous cases of acquired haemolytic anaemias in which the direct Coombs test was positive had shown similar behaviour, and, though the strength of the reaction varied, eluates from previous cases showed the same lack of specificity as the eluates prepared by Kidd (unpublished observation).

The serological findings in the case described below are remarkable in that the antibody both in the serum

and in the eluate from the cells has been shown to be specific against a well-defined blood-group antigen which is also present on the patient's cells.

Case History

The patient was a male clerk aged 32 when first admitted to the General Hospital, Birmingham, in September, 1941. He complained of a painless lump on the foreskin of a few weeks' duration. Mr. Welsh performed a circumcision and local resection of the lesion, which proved histologically to be an epithelioma. The excision was followed by deep *x*-ray therapy administered locally. In 1942 he was admitted as an emergency to another hospital following accidental carbon monoxide poisoning, and has suffered a winter cough since that time. He was confined to bed during the first four months of 1946 with symptoms attributed to acute bronchitis. A radiograph of the chest in January, 1947, showed some shadowing of the right lung field. No cause for this was ascertained. A further radiograph, some four months later, showed partial resolution of the shadowing. In July, 1948, there was a recurrence of the lump on the penis. This failed to respond to deep *x*-ray therapy, and Mr. Welsh performed an amputation of the penis in November, 1948. Microscopy again revealed an epithelioma. At no time was there any evidence suggesting the presence of metastases. Haematological examination at the time revealed: red cells, 5,670,000; Hb, 16.5 g.% (112%); C.I., 1.0; white cells, 7,300, with a normal differential count.

The patient first attended Professor A. P. Thomson's outpatient clinic on December 17, 1950. He complained of lack of energy and dyspnoea on exertion. Both symptoms had been present for two years and had become rapidly worse during the previous two months. Examination revealed a pale, slightly jaundiced man aged 41, with moderate finger-clubbing. The spleen was palpable two finger-breadths below the costal margin. A few rales were present in the right side of the chest. No further abnormal physical signs were elicited. The urine was free from albumin and contained an excess of urobilinogen. There was no family history of anaemia or jaundice. Apart from the history stated above he had suffered no serious illnesses. A tentative diagnosis of haemolytic anaemia was made and the patient was admitted for further investigation.

Investigations.—Blood: red cells, 3,510,000; Hb, 11 g.% (74%); C.I., 1.05; white cells, 9,600 (polymorphs 83.5%, eosinophils 1%, lymphocytes 10%, monocytes 3.5%, N. metamyelocytes 1.5%, N. myelocytes 0.5%); platelets, 189,000 per c.mm.; reticulocytes, 19%. Saline fragility test:—patient: commencing haemolysis, 0.68%; complete haemolysis, 0.32%. Control: commencing haemolysis, 0.48%; complete haemolysis, 0.32%. Direct Coombs test, positive; Donath–Landsteiner test, negative; acid haemolysins, negative; cold agglutinins at 5° C. were positive to 1:32; Wassermann and Kahn reactions, negative. Bacteriological and viral serological studies were negative for leptospirosis; influenza; Q fever; psittacosis, L.G.V.; and streptococcus M.G. Malaria parasites were not seen. Sickling of the red cells was not found. Sternal marrow films showed hypercellularity and erythroid hyperplasia. Serum proteins, 6.37 g. (albumin 4 g., globulin 2.37 g.); serum bilirubin, 1 mg. per 100 ml. Direct van den Bergh reaction negative. A radiograph of the chest showed "some consolidation in the right upper lobe with a small effusion at the right base." Repeated sputum tests for tubercle bacilli and malignant cells were negative.

The patient was discharged three weeks after admission, with a diagnosis of acquired idiopathic haemolytic anaemia. The changes in the lung were thought to represent fibrosis with bronchiectasis following pneumonia in 1946.

Progress

March, 1951.—The patient was readmitted to hospital, complaining of right-sided chest pain of six weeks' duration. Examination revealed the presence of a large right pleural effusion, and 45 oz. (1,300 ml.) of straw-coloured fluid was aspirated. It was sterile and contained 85% lymphocytes and 15% polymorphs. The blood count was essentially the same as that seen on the first admission. A further radiograph of the chest, after aspiration of the effusion, showed an increase in shadowing on the right side.

August, 1951.—The patient was readmitted. His general weakness had increased for three months. A blood count showed a haemoglobin value of 9.7 g.% (66%) and reticulocytes 19.4%. A further radiograph revealed no change in the pulmonary shadows. In view of his continued ill-health, splenectomy was performed on August 31 (Mr. Watson). The spleen was easily mobilized and removed. It weighed 700 g. and histological examination revealed gross engorgement with red-blood cells which largely obliterated the normal splenic architecture. There was no other recognizable abnormality.

After splenectomy his condition rapidly deteriorated and the haemoglobin value fell to 4.7 g.% (32%) by September 10. A pint (570 ml.) of compatible blood was obtained with great difficulty (see below), and following transfusion the haemoglobin rose to 6.8 g.% (46%). By this date the jaundice, which was only slight before splenectomy, had become pronounced. The motions were now pale and the urine contained bile pigments. Four days later a femoral vein thrombosis was noticed, and sudden onset of severe pain in the left chest suggested a pulmonary embolism. Two days later (September 16) he complained of upper abdominal pain. The liver could be palpated a hand's breadth below the costal margin. The neck veins were not distended. Within a few days his condition became critical. We were unable to obtain further compatible blood at this time, and from September 18 to 24 800 mg. of cortisone was given intramuscularly. His condition began to improve rapidly, and the haemoglobin value, 6.8 g.% (46%) on September 15, rose to 8.8 g.% (60%) by October 19. By this time the liver had returned to normal size and the jaundice had decreased. Liver function tests on October 2 had shown an immediate positive van den Bergh reaction with a serum bilirubin of 2 mg. per 100 ml., total serum protein of 6 g.% (albumin 3.2 g. and globulin 2.8 g.), serum alkaline phosphatase 18 units, thymol turbidity 10 units, thymol flocculation +++, and colloidal gold ++++. The patient improved sufficiently to return home on October 24, approximately two months after splenectomy.

September, 1952.—He was readmitted as an emergency case. His condition had remained fairly stationary until ten days before admission, when he suffered a sudden severe relapse. On admission he was critically ill, and the haemoglobin value had fallen to 3.2 g.% (22%). He was deeply jaundiced, the liver was very much enlarged, and the legs were oedematous. The neck veins were not distended. The urine contained large quantities of bile pigment and urobilinogen. A pint (570 ml.) of compatible blood was transfused on September 19 and a further pint on the following day. Cortisone therapy was started on September 19. Liver-function tests on September 22 were as follows: strongly positive direct van den Bergh reaction; serum bilirubin, 48 mg. per 100 ml.; serum proteins, 5.5 g.% (albumin 2.6 g., globulin 2.9 g.); serum alkaline phosphatase, 16 units; thymol turbidity, 8 units; thymol flocculation ++; and colloidal gold ++++.

Cortisone therapy was continued in a daily dosage of 100 mg. by mouth. The patient's condition gradually improved and the jaundice became less deep. By October 20 the liver enlargement had disappeared, the serum bilirubin had fallen to 7 mg. per 100 ml., and the haemoglobin value had risen to 9.7 g. % (66%). On October 27 it was decided to decrease the daily dosage of cortisone gradually, but the patient's condition relapsed almost immediately and the haemoglobin value fell from 9.7 g.% (66%) on October 27 to 5.4 g.% (37%) on November 3. By this date the cortisone had been reduced to 25 mg. daily. The jaundice deepened and the liver rapidly enlarged. In view of this relapse and a temporary shortage of cortisone the patient

was put on A.C.T.H., starting with 25 mg. daily, administered in an intravenous saline drip. The dose was increased gradually to 40 mg. This induced a further remission, and the haemoglobin value, 5.1 g.% (35%) on November 5, rose to 10.5 g.% (71%) three weeks later.

Material and Methods

Direct Coombs Test.—This was performed on cells washed three times in saline.* They were put on an opaque tile and mixed with an equal amount of suitably diluted anti-human globulin serum.† Tests were read after two and five minutes, using a hand lens (×8). All tests were performed alongside suitable controls, which included AB rhesus-negative cells washed three times in saline and the patient's own cells, to which was added saline instead of anti-human globulin serum.

Rhesus Typing.—The following sera were used for the determination of the genotype of the patient and his family: anti-C, anti-C+, anti-C^w, anti-D, anti-E, anti-c, and anti-e, the latter containing a trace of anti-C. All the tests were run off with suitable controls.

Investigation for Presence of Antibodies.—The antibodies contained in both serum and eluates were investigated by means of a large panel of fully typed cells which were used in saline and albumin suspension and also used by means of the indirect Coombs test.

Indirect Coombs Test.—This was performed as follows: 1 volume of washed cells was mixed with 5 volumes of serum or eluate, thoroughly mixed, and incubated for at least two hours at 37° C. The supernatant was then removed and the cells were washed in saline three times. For reading, the same procedure was followed as in the direct Coombs test.

Preparation of Eluates.—The eluates were prepared from cells washed at least three times and then packed tightly. After the last wash the supernatant saline was removed and a volume of fresh saline equal to the volume of packed cells was added. The eluates were prepared at both 56° C. and 37° C. At the higher temperature the sample was submerged in a 56° C. water-bath and kept there with frequent agitation for approximately 30 minutes. It was then rapidly centrifuged and the supernatant removed. For the preparation of the eluate at 37° C., the cells were treated as before, and the specimen was then put into a 37° C. incubator overnight. Immediately on being taken out of the incubator it was centrifuged and the supernatant removed. The eluates were removed immediately after spinning and stored at −15° C. until used. The eluates prepared in either way showed heavy haemolysis. Generally speaking, eluates prepared at 37° C. worked better than those prepared at 56° C.

Results

Serum.—When it became necessary to transfuse the patient it was found that the serum contained an antibody active at 37° C. against saline- and albumin-suspended cells. It also gave a positive indirect Coombs reaction against the same cells. A large panel of cells was then used, and it was found that at 37° C. only one cell sample (cDE/cDE) was not agglutinated. Identical results were obtained in the indirect Coombs test. As the serum also contained an unspecific "cold" agglutinin it was necessary to incubate all tests carefully. These results were strongly suggestive of the presence of an anti-e in the serum, as no other antigen could be found which was common to the agglutinated cells and lacking from the cells in question. This was confirmed later when a further eight samples of this subtype (cDE/cDE) became available for testing. The titre of the antibody determined against albumin suspended cde/cde cells was 16 and against cDE/cde 4 (double-dose effect) (Race and Sanger, 1950). A very careful history obtained from the patient and his parents and wife showed, surprisingly, that he had never been transfused or received blood injections.

The eluates prepared from several specimens of the patient's cells in the course of his illness gave identical results. They could be made to act mainly by means of the indirect Coombs test, but weak reactions were also obtained when they were investigated with saline- and albumin-suspended cells. The eluates showed the same pattern of reaction as the serum. All cells containing the e antigen gave, when incubated with the eluates, a positive Coombs reaction, whereas E/E cells obtained from various donors always gave a negative result. The identity of the antibody, coated on to the cells and present in the serum, could thus be proved.

Direct Coombs Test.—At all times the cells of the patient showed a strongly positive direct Coombs reaction.

Group and Genotype.—In view of the presence of the antibody described above, it was of more than theoretical importance to define precisely the genotype of the patient. As pointed out, the serum contained a low-titred "cold" agglutinin and the cells persistently showed a moderate degree of auto-agglutination. This was abolished by washing the cells in 56° C. saline, and typing was then facilitated. The following results were obtained: the group was determined as Group O but was not confirmed by serum grouping, as no Group A or Group B donors were found of the subtype cDE/cDE. (All others, of course, showed agglutination due to the presence of the anti-e.)

Genotype.—The cells were agglutinated by anti-C, anti-C + anti-C^w, anti-D, and anti-e, but were not agglutinated by anti-E and anti-c. These results suggested that the most likely genotype was CDe/CDe. It was astonishing to find this genotype in view of the presence of the antibody already found in the patient's serum and on his cells, and it was therefore decided to investigate fully the available members of his family. Their groups and reactions are summarized in the Table. The sera of all members of the family were investigated, but showed no deviation from the norm. The family investigation thus supports the view that the genotype of the patient was CDe/CDe. It is of interest that the cells from all members of the family showed typical behaviour with the antisera available and did not give the impression of containing allelomorphic antigens. We are greatly indebted to Dr. R. R. Race, who was kind enough to check the results and to determine the other antigens on the patient's cells. The cells from the specimen of the patient were found to be M+, N+, S+, P+, Lu(a−), Le(a+ b−), Fy(a−). After the patient had received several transfusions with cDE/cDE cells these cells survived for a considerable period and did not clump on the addition of anti-human globulin serum. The blood transfusions gave rise to no reactions.

The Rhesus Types and ABO Groups of the Patient's Family

	ABO Group	Anti-C*	Anti-C+C^w†	Anti-D‡	Anti-E†	Anti-c†	Anti-e†	Probable Genotype
Patient	OO	+	+	+	−	−	+	CDe/CDe
Father	AO	+	+	+	−	+	+	CDe/cde
Mother	OO	+	+	+	+	+	+	CDe/cDE
Sister	AO	+	+	+	+	+	+	CDe/cDE
Sister	OO	+	+	+	−	+	+	CDe/cde
Brother	AO	+	+	+	−	−	+	CDe/CDe

* One example. † Two examples. ‡ Three examples.

Discussion

It is obvious that an antibody present in the serum of a patient will combine with its homologous antigen. The best example is perhaps the serology as seen in the haemolytic disease of the newborn when an antibody (usually anti-D) which has been passively transmitted to the patient via the placenta combines with its homologous antigen (D). The recognition of the union of antibody and antigen was made possible by the introduction of the Coombs test, which

*Freshly prepared 0.9% saline was used throughout this investigation.

†Anti-human globulin serum was kindly supplied by Dr. A. E. Mourant, of the Lister Institute.

demonstrates the presence of antibody globulin on the surface of the cells. Uncoated cells have always given a negative result. The positive direct Coombs reaction found in cases of acute acquired haemolytic anaemia is therefore taken to indicate the presence of antibody globulins on the surface of the cells. The presence of antibodies in the serum of these patients lends further support to this assumption.

The antibodies present in the serum and in the eluates in acquired haemolytic anaemia have previously been regarded as unspecific, or pan-agglutinins. The diagnosis of the specificity of an antibody depends naturally to a great extent on the size of the available panel of test cells. In our case the diagnosis could only be made through the availability of a cDE/cDE donor. As this subtype is comparatively rare among the British population (1.99%) (Race *et al.*, 1948), it is conceivable that even a large laboratory might not have this particular test cell available. As Kidd (1949) has pointed out, these antibodies were regarded as anti-species-specific, as in his cases no cell could be discovered which would not have been acted upon by the eluates. The test cell which permitted the diagnosis of the specificity of the antibody in our patient is, however, usually available in specialized laboratories. An antibody defining, for instance, the very frequent antigen Tj^a (Levine *et al.*, 1951) would react with all available test cells, as this antigen is so widely distributed and a cell lacking it might not be available at all. A pan-agglutinin would therefore be assumed.

Further difficulties might arise if several antibodies were formed against a variety of antigens. Very carefully performed absorption experiments and choice of test cells would be necessary to differentiate the various antibodies contained in any one serum or eluate. Multiple antibody formation is, of course, well known (Callender, Race, and Paykoc, 1945; Malone and Cowen, 1950).

It has been assumed in the past that no organism will form an antibody against an antigen carried on any of its own circulating cells (horror autotoxicus). This was taken to be a basic "law" of serology (Boyd, 1947). Our case has shown that an organism is capable of forming an antibody active against its own antigens, and the serology of acquired haemolytic anaemia would seem to show that this happens in all these cases. The antibodies attached to the cells and/or present in the serum of these patients must have combined with one or more antigens on the cell surface. Our case is exceptional in one way only—namely, that we were able to define the antigen precisely. Dameshek and Schwartz (1940) have shown that injection of antibodies directed against the cells of their experimental animals produce haemolytic anaemias typical in all respects. It is conceivable that the presence of antibodies in patients with acquired haemolytic anaemia may be the cause of these anaemias, though cases have been known in which, in spite of the persistent direct Coombs reactions, patients have had complete remissions. Further work would seem to be necessary to elucidate fully the mechanism of these types of haemolytic anaemias.

The presence of these antibodies in the serum and on the cells of the patients suffering from acquired haemolytic anaemia is difficult to explain. A tentative explanation might perhaps be offered as follows. It is a common experience that many haemolytic anaemias of the acute and acquired type are initiated by an acute febrile episode sometimes accompanied by the signs and symptoms of an upper respiratory tract infection. One might postulate that these initial febrile episodes have been caused by an agent, possibly viral, which carries an antigen similar in its structure to that present on the cells of the patient. An antibody formed in response to the stimulus of this infecting agent might cross-react with an antigen chemically related to the antigen which stimulated its production. There need not be a biological relationship between the two antigens. Many viral and rickettsial infections are known to produce antibodies which cross-react with unrelated organisms—Weil–Felix reaction and biological false Wassermann reactions after vaccinia and other viral infections (Moore and Mohr, 1952). (In this connexion one might point out that unspecific positive Wassermann reactions are not uncommon in cases of acquired haemolytic anaemia.) This applies particularly if the infection is severe and if the immunizing stimulus has been applied repeatedly. It is common serological experience that repetitive stimulation with one agent produces antibodies which are less specific than antibodies produced with fewer immunizing stimuli. It could also be possible that this antibody production may be initiated by a different pathological process, and the case of Levine *et al.* which produced the anti-Tj^a was shown to be suffering from a neoplasm which specifically absorbed the antibody, the patient's cells lacking the antigen.

Summary

A case of acquired haemolytic anaemia presenting a variety of interesting clinical details is described.

The development of an anti-e in the presence of the homologous red-cell antigen without stimulation by transfusion or blood injection was shown.

The serological findings were discussed and a tentative explanation was offered.

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DIAGNOSIS OF "SEDORMID" PURPURA

BY

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Thrombocytopenic purpura following ingestion of the hypnotic "sedormid" (allyl*iso*propylacetylurea) by susceptible individuals is a well-known clinical entity. The pathogenesis of this syndrome was made clearer by the investigations of Ackroyd (1949b, 1949c, 1949d) on three patients who had recovered from such attacks. As a result of his researches, he put forward the hypothesis that thrombocytopenia in these patients was associated with a circulating substance in the blood which, in the presence of sedormid, caused lysis of platelets (Ackroyd, 1949d). This lysis he observed to take place *in vitro*, using suitable preparations of the patients' blood. An alternative method of demonstrating platelet lysis was by using the indirect approach of estimating clot retraction either of whole blood or of plasma. In his patients clot retraction was very much, and consistently, reduced in the presence of sedormid. The value of such tests as these obviously lies in enabling confirmation of the provisional diagnosis to be made without the necessity of

giving a test dose of the drug by mouth. This last method, which in the absence of satisfactory *in vitro* tests is the only way of arriving at a definite diagnosis, is not without danger. Use of this test is also limited, as in one of our cases, by the patient's refusal to submit to a test dose.

It is important from the practical point of view, as well as academically, to make the correct diagnosis in suspected cases of sedormid purpura. In the absence of special measures, as outlined above, the historical sequence of events is all-important in diagnosis. The history of sedormid administration may, however, be merely coincidental. It is therefore of great advantage to be able to reassure the patient that no recurrence will take place provided no more sedormid is taken. Inability to give this reassurance demands a further search for an aetiological basis for the purpura.

In two years six cases with the provisional diagnosis of purpura due to sedormid were referred to this unit. I attempted to confirm the diagnosis in all, both by *in vitro* tests using, in the main, clot-retraction estimations, following the method of Ackroyd (1949a), and by skin patch tests. Test doses were used only in some of the cases. In two cases alone was unequivocal confirmation obtained from *in vitro* tests. The possible reasons for this failure are discussed, and a modified approach to the *in vitro* investigation of patients suspected of having sedormid purpura is suggested.

Case 1

A married woman, separated from her husband, was first seen in October, 1949, when she was aged 29. She had taken 1½–2 tablets of sedormid every night without fail for the previous seven months, the last dose of two tablets two nights before admission. After having taken the tablets for about two months, she noticed that she bruised very readily with slight trauma and sometimes even without apparent trauma. She had never before bruised easily. In addition, she developed a reddish speckled rash, particularly on the legs. The bruising and rash persisted with little change, except that in the ten days before admission both became more pronounced. A menstrual period one week before admission was more profuse than any she had experienced before. A blood film examined a few days before admission showed platelets so scanty as to be almost absent.

On admission several bruises were found; there was a petechial rash over the body, mainly on the legs, and slight oozing occurred from the gums. The positive-pressure capillary fragility test (Bell, Lazarus, and Munro, 1940) was moderately positive. A patch test of sedormid in propylene glycol, after the method of Ackroyd (1949b), was applied for three and a half days. There was no petechial reaction. Three days after admission her platelet count was 60,000, and after a further week it was 300,000. One week later, when the platelet count was 290,000, the clot retraction of whole blood by the method of Macfarlane (1939) was carried out, both in the presence of sedormid and with a normal-saline control. In the presence of sedormid, clot retraction was reduced by 16%. She did not develop any further bruises or petechiae after admission, and her capillary fragility returned to normal. The patient was discharged home.

When seen four months later there had been no further purpuric episodes. Menstrual periods had again become scanty. Her platelet count was 310,000. After a further three months she was readmitted, having for the past two weeks had a recurrence of the rash on her arms and bruises on her legs and arms. A recent menstrual period had again been associated with excessive loss. She denied, however, taking any more sedormid. Her platelet count on admission was 220,000, and after a few days her petechiae and bruises had subsided. She then had a menstrual period, normal for her, lasting only a few hours. A patch test was again negative. Clot-retraction studies by the method of Macfarlane showed very slight reduction in the presence of sedormid. When these tests were repeated about a week later, using the method of Ackroyd (1949a), no reduction could be demonstrated. During the following five months she developed occasional crops of petechiae, mainly on the wrists and hands, and occasionally suffered apparently spontaneous bruising. However, her platelet count was always of the order of 200,000, and, apart from "spots" on the skin which might or might not have been fading petechiae, no purpuric manifestations were ever observed by us.

In June, 1951, she was admitted for trial of sedormid by mouth. Patch test and intradermal tests with the drug were negative, and no *in vitro* sensitivity could be demonstrated. She was first given a test dose of half a tablet (0.125 g.). No fall in platelet count was observed. The next morning she was given two tablets. No fall in platelet count or reduction in plasma clot retraction was observed, and there were no purpuric symptoms or signs. After a further interval of five months she was again admitted for a trial of sedormid in bigger dosage. A total of 67 tablets was given over a period of 14 days. Her platelet count and clot retraction remained unchanged. Aspiration of sternal marrow revealed no abnormality.

Case 2

A man, aged 33 when first seen in June, 1950, began to take sedormid in March, 1949, consuming 20 tablets during that and the succeeding month. About that time he noticed on both legs below the knees a dark "spotty" rash, which passed away quite rapidly. He did not take any more tablets, apparently, until the middle of May, 1950, when in four weeks he took 20 tablets. There was then an interval of a few days and he again took sedormid. After a further eight tablets he noticed a recurrence of the rash on the legs. There was no history of ready bruising. He was not sure when he had last taken sedormid, but it was probably two days before admission. Apart from a florid petechial rash on the lower legs, no abnormality was found on physical examination. Capillary fragility by the positive-pressure test was normal, and the platelet count was 190,000. Two weeks after admission clot retraction by the method of Macfarlane was significantly reduced (greater than 10%) in the presence of sedormid. Repetition of these studies four days later showed no such reduction. Clot retraction by the method of Ackroyd after a further two days again showed no reduction with sedormid. The petechiae subsided without any further lesions appearing. The patient reported on one occasion, two months after discharge from hospital, and apparently had had no recurrence of the "rash."

Case 3

A married woman, aged 48 when first seen in March, 1951, had been taking sedormid tablets on rare occasions over the past ten months, and seven days before admission she again took one tablet at night-time. On the following day she developed petechiae on legs and arms, the shoulders, and the interscapular region. There was gross spontaneous bruising in both thighs, the right upper arm, and the left forearm. She was found to have thrombocytopenia. On examination the bruises and petechiae were seen to be subsiding, and no fresh lesions were appearing. Plasma clot retraction by the method of Ackroyd revealed no *in vitro* sensitivity to sedormid. A patch test was negative. She was not seen again for eight months. In the interim, left nephrectomy had been performed for hydronephrosis without untoward incident. She had had no further petechiae. Repetition of plasma-clot-retraction tests again gave negative results. Platelet counts were of the order of 160,000 to 180,000.

Case 4

A widow, aged 55 when first seen in April, 1951, had been taking sedormid off and on for about four and a half years, and ten months before being seen began to take 1–1½ tablets regularly every night. After about one month she began to develop large bruises on her arms and legs, apparently unrelated to trauma. Six months later she was told that sedormid might be responsible for her symptoms, and she ceased to take the drug. After this the tendency to easy bruising went away and did not return.

Repeated tests on plasma for *in vitro* sensitivity were all negative, as were patch tests. She was therefore admitted to hospital for test dosage. After an initial dose of half a tablet (0.125 g.) had been taken without effect, the dosage was continued. In 14 days she had had 21½ tablets. There was no subjective or objective evidence of thrombocytopenic purpura.

Case 5

A married woman aged 30 was first seen on August 17, 1951. She had started to take sedormid some six to nine months previously, and thinks that she consumed, in all, the contents of three to four boxes containing 20 tablets each. The tablets were taken at quite irregular intervals. On August 9, after an interval of some weeks, she recommenced taking sedormid more regularly than she had ever done before—namely, one tablet every night. On the evening of August 13 she took two tablets. Early next morning, at about 4 o'clock, she awoke to find blood clot inside her lower lip. A few hours later she noticed spots like "blood blisters" on her fingers and hands. By the afternoon bruises had begun to appear on her arms, legs, and body, quite unrelated to trauma, and she suffered a spontaneous nose-bleed. Normally she does not bruise easily, nor is she subject to nose-bleeding. "Blood spots" and bruises continued to appear throughout that day and into the following day. She had taken no more tablets. On her admission to hospital she was seen to have haematuria, in addition to the above findings, and a little bright blood was noticed in her stools. She had felt nauseated but had not vomited. A blood film was examined and platelets were almost absent. Some 24 hours later blood was taken, using 3.2% sodium citrate as anticoagulant (Ackroyd, 1949c). Plasma-clot-retraction tests were carried out in triplicate, using a saturated sedormid solution in normal saline against normal saline controls (Ackroyd, 1949c). The results were as follows: saline control, 90% retraction; sedormid preparation, 40% retraction.

There was no further bleeding, bruising, or spots, and on August 20 plasma clot retraction gave the following results: saline control, 89% retraction; sedormid preparation, 76% retraction. The next day the platelets numbered 300,000 per c.mm. A patch test was applied to the inner surface of the right arm, consisting of a saturated solution of sedormid in propylene glycol (Ackroyd, 1949b), and a similar control patch of propylene glycol was applied to the left arm. The patch test was examined (after 48 hours) on August 22. There was no reaction at all in either patch or control. Plasma clot retraction was repeated on this day with the result: saline control, 93% retraction; sedormid preparation, 92% retraction. In all these preparations the plasma was allowed to stand in contact with the test solution for 15 minutes before clotting with thrombin.

She was next seen as an out-patient on October 23. She had been in perfect health, with no recurrence of purpura. She had had no more sedormid. Her platelet count was 170,000 per c.mm. and her blood count was normal in all other respects. Platelet counts on October 30 and November 5 were 380,000 and 160,000 per c.mm. respectively. On the latter day plasma clot retraction was repeated: saline control, 90% retraction; sedormid preparation, 93% retraction. On November 13 the platelet count was 150,000 per c.mm. and plasma clot retraction was saline control, 89%; sedormid preparation, 88%. It had been proposed to administer a small test dose of pure allyl*iso*propylacetylurea corresponding to about one-eighth of a tablet (Moeschlin, 1942). The patient declined this and further tests, and she has not been seen since.

Case 6

A widow aged 69 was first seen on January 16, 1952. Some one and a half to two years previously she had taken an unknown number of sedormid tablets over a period of a few weeks. She then changed her sedative to phenobarbitone, which she took regularly every night. Of the old stock of sedormid there remained two or three tablets in a bottle, which was then filled with phenobarbitone tablets. In the course of consumption of the contents of this bottle she thinks that two, or possibly three, tablets of sedormid were taken, one on each evening of January 11 and 12, and possibly again on the 13th. About mid-day on the 13th small black lumps like "blood blisters" appeared on her tongue. Red spots and bruises then began to develop spontaneously all over her body. Her tongue bled and purpuric spots appeared on her palate and pharynx, making swallowing painful. She had never before been subject to any abnormal bleeding tendency.

The next day the blood count was normal, apart from a platelet count of 48,000 per c.mm. Purpuric spots and bruises continued to appear, and a further platelet count on January 16 gave 15,000 per c.mm. Occult blood was present in the faeces on this day, but there was no haematuria.

On the 17th her platelet count was 67,000 per c.mm. and plasma-clot-retraction tests were saline control, 83%; sedormid preparation, 18%. Next day her platelets numbered 126,000 per c.mm. and clot retraction was saline control, 84%; sedormid preparation, 33%. A patch test, applied on January 17, was negative after 96 hours. She had now ceased to develop fresh purpuric lesions, and platelet counts continued to rise, being 200,000 per c.mm. on January 21 and 371,000 and 360,000 on succeeding days. Clot-retraction tests still showed sensitivity on January 19: saline control, 83%; sedormid preparation, 54%; but by January 23 had become normal: saline control, 87%; sedormid preparation, 86%. After one month, during which time she had been free of all symptoms, clot-retraction tests were repeated and, to our surprise, gave the following result: saline control, 86%; sedormid preparation, 56%. The patient stated that she had not knowingly taken sedormid in the interim. Unfortunately, it has not been possible to perform further tests, and this apparent return of *in vitro* sensitivity to sedormid remains unconfirmed and unexplained.

Discussion

There are certain obvious criticisms which arise at once in discussion of these cases. The most obvious and most important one is that they may not in fact represent cases of purpura due to idiosyncrasy to sedormid. This diagnosis is, in the main, a presumptive clinical one, with the exception of those cases in which, if we accept the validity of Ackroyd's work, positive *in vitro* tests have been obtained. At first I was reluctant to administer a test dose to these cases in view of the possibility of arousing a dangerous, even fatal, reaction. For some time I persisted in this attitude, even in the face of negative *in vitro* and patch tests, for I felt that failure to produce positive findings here might have been due to technical imperfections. This aspect still remains, perforce, a matter for possible criticism.

With regard to the disappointingly negative results when test-dosing was at length employed, I was encouraged to some extent by reading of the experience of Falconer and Schumacher (1940). These authors gave test doses of half a tablet and two tablets on successive days to a patient with sedormid purpura who had been free of purpuric manifestations for scarcely a week. A strong positive response was obtained after the second test dose. A little more than a

year later the same patient was again given sedormid. On this occasion, however, it was not until a total of 11½ tablets had been taken over a period of nine days that haemorrhagic phenomena associated with marked thrombopenia appeared. In most reported cases it seems that the test dose has been administered shortly after recovery from an attack of purpura, and this may account for a correspondingly high proportion of positive results.

In Case 1 the first test doses were not given until some 20 months had elapsed after sedormid had apparently last been taken. Case 4, which was a very mild case, showing bruising as the only symptom, was not given a test dose until eight months after the last dose of sedormid. It seems not beyond possibility that such intervals of time might have allowed an acquired sensitivity to sedormid to disappear completely.

If, then, we assume that sensitivity to sedormid by mouth can diminish considerably, or even disappear altogether with the passage of time, this reasoning may surely apply equally well to *in vitro* tests. Ackroyd (1949b) says, "Hypersensitivity, once it has been established, persists for an unknown, but often considerable, period," and refers to one of his cases in which hypersensitivity was found nine years after the original attack of purpura. It appears (Ackroyd, 1949d) that he was able to demonstrate *in vitro* sensitivity in his patients, at periods ranging from 28 months in his Case 3 and 50 months in his Case 1 to some 112 months in his Case 2. The interval in his Case 2 was probably less than this, for he mentions inducing an experimental attack of purpura after December, 1940, the last recorded time of an attack due to sedormid.

The usefulness of both *in vitro* tests and the giving of a test dose in confirming a provisional diagnosis of sedormid purpura depends, therefore, on the length of time that sensitivity persists after subsidence of the purpura. If this interval is relatively long, to be measured in months or years, then there is no need for undue haste in performing the tests. If, on the other hand, the sensitivity passes off in a matter of days, as it certainly appeared to do in Case 5 above, and probably in Case 6, then *in vitro* tests should preferably be carried out as soon as possible and at the height of the purpuric attack. In Case 5 the first estimation of plasma clot retraction was performed four days after the last dose of sedormid. Clot retraction in the control specimens was normal, but in the presence of sedormid it was reduced by 50%. Three days later the reduction had fallen to 13%, and two days after this there was no reduction. All subsequent tests were negative. Case 6 followed an essentially similar pattern, except that there was an apparent return of sensitivity one month after tests had become normal. These results indicate a steadily decreasing sensitivity over a period of a few days. After experience with these cases, I referred again to our Cases 1 and 2. In both of these a reduction of clot retraction in the presence of sedormid (using the method of Macfarlane) had occurred. As this reduction had been found only during the earlier stages of the purpura, and later vanished entirely, I had been inclined to discount the results. In view of the later findings in Cases 5 and 6, I now feel that perhaps the results in Cases 1 and 2 were valid after all.

I may mention here, in passing, that I have never had a positive sedormid response in clot-retraction estimations performed on patients with florid purpura due to other causes —for example, aplastic anaemia, leukaemia.

My findings, therefore, are somewhat at variance with those of Ackroyd. From his work it would appear that there need be no undue haste in the attempt to make a retrospective diagnosis of sedormid purpura, because of the long duration of sensitivity in his patients. From my work it seems that the sensitivity may be of relatively short duration. To avoid, therefore, the possibility of, as it were, "false negative" *in vitro* tests, I venture to suggest that such tests be carried out as soon as the provisional diagnosis of thrombocytopenic purpura due to idiosyncrasy to sedormid has been made.

Summary

The use of *in vitro* tests in the diagnosis of sedormid purpura is discussed.

Evidence is presented that sensitivity to sedormid, presumed to be due to a plasma factor in the blood of patients recovered from sedormid purpura, may be of short duration.

It is therefore suggested that *in vitro* tests be carried out on the patient as soon as the provisional diagnosis of sedormid purpura is made, and preferably at the height of the purpura.

I wish to thank Dr. C. R. Bickerton Blackburn, Director of the Clinical Research Unit, Royal Prince Alfred Hospital, for permission to publish the case reports, and for his constant help and encouragement. I also thank Drs. E. L. Susman, A. W. Morrow, F. L. Ritchie, F. C. Hughes, M. S. Richmond, and R. W. Fay for referring cases. In particular I thank the staff of the Haematology Department of the Fairfax Institute of Pathology, Royal Prince Alfred Hospital, for carrying out all platelet and other blood-cell counts, and Dr. W. J. Hensley, registrar in the Clinical Research Unit, who assisted in the laboratory and clinical investigations.

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AN OUTBREAK OF TRICHINIASIS IN BARRY, GLAMORGAN

IMPROVED TECHNIQUE FOR DEMONSTRATION OF TRICHINELLA IN MUSCLE

BY

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In May, 1952, an outbreak of trichiniasis occurred in the Borough of Barry, Glamorgan (population 41,000), in which at least 25 people were affected as a result of eating pork sausage-meat. We report this outbreak not only because of its size but also because the infected pigs came from a district which has been incriminated on six previous occasions, resulting in 47 human cases. Hitherto, trichinellae have not been demonstrated in pigs or rats in the district (Howell, 1941, 1942), but, arising out of the inquiries into the present outbreak, it was possible to demonstrate live trichinellae in rats and pigs from the suspected area. We do not propose to review the literature of trichiniasis in Britain, as this has been done recently by Young (1947).

The Outbreak

On May 3, 1952, two persons were seen by their doctors with symptoms suggestive of trichiniasis. Inquiries amongst the other practitioners in the area revealed a further 23 patients with a similar illness. All except one admitted eating sausage, sausage-meat, or Scotch eggs within three weeks of the onset of symptoms. The sausage and sausage-

meat were obtained from one or other of two pork butchers, and the Scotch eggs were prepared in a local café from sausage-meat obtained from one of the butchers. One patient had eaten raw sausage-meat.

Between March 28 and April 26 182 pigs were slaughtered at Barry abattoir and 31 carcasses were received from other areas. With the exception of three carcasses, graded as "manufacturing meat," all the pigs came from the town's usual source of supply, the Vale of Glamorgan. The three pigs which were used for the manufacture of sausage-meat came from West Pembrokeshire, and it was shown that on April 4 one of these carcasses had been divided between the two butchers whose sausage-meat was incriminated in the outbreak. Between March 29, when the pigs were slaughtered, and April 4 the pigs had been kept in storage at −6° C. The sausages were on sale between April 7 and 11 and possibly on the 15th and 16th. By the time the existence of the outbreak was realized it was not possible to obtain samples of the suspected meat.

Incubation Period.—In 17 of the patients it was possible to estimate the incubation period, which ranged from 11 to 27 days. In 14 (82%) the first symptoms came on between the 15th and 24th days.

TABLE I.—*Age and Sex Distribution*

Age	Male	Female	Total
0–9	—	—	—
10–19	1	—	1
20–29	—	1	1
30–39	4	12	16
40–49	1	4	5
50–59	1	—	1
60–69	—	1	1
Total ..	7	18	25

Age, Sex, and Income Level.—It was remarkable that 16 of the 25 patients were between 30 and 40 years of age and a further 5 between 40 and 50 (Table I). There did not appear to be any tendency to involve one social class.

Mortality.—There were no deaths, although at one time two patients were critically ill. A feature of the disease in Britain is that there is a low mortality as contrasted with case fatality rates of 16–30% in Germany and 3–10% in the United States. This may be due to the fact that pork is not eaten raw in this country, and thus the infecting dose is smaller.

Symptoms.—Table II shows the frequency of the main symptoms encountered. The typical history, described in early accounts, of gastro-enteritis followed by oedema and muscle pains was seen in only four patients, the most common presenting symptoms being periorbital oedema. This agrees with the findings in outbreaks described in recent years in this country and in the United States. The duration of symptoms was four to nine weeks, but 14 patients reviewed after 18 weeks still complained of some muscle pain and lassitude.

TABLE II.—*Frequency of Symptoms*

Symptoms	No. of Cases	Percentage
Periorbital oedema	25	100
Muscle pains	24	96
Fever	11	44
Headache	10	40
Neck pain and stiffness	6	24
Diarrhoea	4	16
Abdominal pain	4	16
Vomiting	3	12
Oedema of limbs	2	8
Conjunctival haemorrhage	1	4

Laboratory Findings

Eosinophilia.—Differential counts were made in all the cases described (see Table III). In cases in which repeated counts were done the highest percentage of eosinophils obtained was recorded. Of the 25 cases, 20 showed an eosinophilia of 10% or over within seven days of onset of the illness and the remaining five developed eosinophilia within a further week. These results substantiate the opinion that the most useful single test in the diagnosis of trichiniasis is the eosinophil count, done either as a differential or, preferably, as a total count. Although cases of trichiniasis have been reported without eosinophilia they are rare, and unless the parasites can be demonstrated in the tissues the diagnosis may be doubted. In none of the patients did examination of the centrifuged deposit of lysed venous blood show the presence of trichinellae.

TABLE III.—*Highest Eosinophil Count in 25 Patients*

Percentage of Total White Cells	No. of Cases	Total Eosinophil Count per c.mm.	No. of Cases
10–19	3	Under 500	0
20–29	6	500–1,000	1
30–39	5	1,000–2,500	3
40–49	5	2,500–4,000	5
50–59	4	4,000–5,500	6
60–69	1	5,500–7,000	6
70–79	1	7,000–8,500	2
		8,500–10,000	2

Skin Tests.—It was possible to obtain enough trichinella antigen to test 12 of the patients selected at random. Of these, nine gave an immediate positive reaction, two a delayed positive reaction (after 24 hours), and one was negative. All tests were done four weeks after onset of symptoms. The one patient who was negative had the highest eosinophil count of all (76%).

Biopsy.—Two patients were admitted to hospital, and in both of these muscle biopsy showed the presence of *Trichinella spiralis* larvae.

Epidemiology

The infected meat was traced back to two pork butchers and through them to one of three sows from small farms in West Pembrokeshire. Both these farms were visited by one of us. It was found that all pig swill was boiled and that trimmings from locally killed pigs were not available as foodstuff. Since it appeared, therefore, that pigs did not become infected by eating uncooked pig tissue it was decided that rats killed on these farms should be examined. Unfortunately only four such rats were submitted, but it was possible, by using the modified technique described below, to show the presence of *T. spiralis* larvae in one of them.

At the same time we arranged to examine diaphragms from pigs from West Pembrokeshire and also from the area which usually supplies Barry—the Vale of Glamorgan. Of 288 diaphragms from West Pembrokeshire, 4 were shown to contain trichinella larvae, whereas none of the 262 from the Vale of Glamorgan were infected.

We believe this is the first time that either rats or pigs in West Pembrokeshire have been shown to harbour trichinellae, although pork from the area has been incriminated on many occasions on epidemiological grounds. It is hoped that in the near future it will be possible to examine large numbers of rats from various districts in order to determine the true incidence of rodent trichiniasis.

Method of Examination of Pigs' Diaphragms and Rats

The method recommended by Young (1947) was tried for the first specimens, but was found difficult because of the persistence in the deposit of a proportion of undigested muscle fibres. By using the modification described below it was found that the larvae showed very active motility when examined at 37° C. This motility, which is not a feature of the original technique, made the demonstration of trichinellae easier.

The porcine specimens were examined in batches of not more than 10. Approximately 5 g. of each specimen was taken and freed from any adhering fat and tendon. The specimens were then pooled and passed through a good-

quality domestic mincer, using the fine-cutting blade. Rats were skinned, the feet cut off, and minced without difficulty. The minced tissue was then placed in an artificial gastric juice consisting of 0.5% pepsin *B.P.* plus 0.5% HCl, between 10 and 12 ml. of fluid being used for each gramme of tissue. The mixture was incubated at 37° C. in a water bath for six hours and stirred every half-hour.

The partly digested tissue was poured through two copper sieves one above the other, the upper one being 44 mesh per inch (0.353 mm. aperture), the lower 120 mesh per inch (0.124 mm. aperture) B.S.S.410/1943. Both sieves were then washed with 1 litre of tap-water at 37° C. The coarse particles contained in the upper sieve were washed back with 500 ml. of the digesting fluid and were incubated for a further four hours at 37° C. The finer deposit from the lower sieve was washed back with 500 ml. of tap-water and kept at 4° C.

The material at this stage consisted of the *T. spiralis* larvae, if present in the original specimen, greatly obscured by fine muscle fibres.

It was found that a further digestion, using pancreatin, 0.2%, and NaOH, 0.2%, for two to three hours at 37° C., removed the remaining fibres completely, leaving nothing but trichinellae. The digest was passed through the finer sieve, washed back with water at 37° C. into a glass Petri dish, and examined under a plate microscope (×40). The active motility of the trichinellae made them easy to recognize.

The value of the modification is shown in the following experiment. Two rats were infected by feeding with tissue containing live trichinellae. They were killed after four weeks and all the muscles removed. The tissues were minced by passing through the mincer three times, after which the finely divided material was thoroughly mixed by stirring. Portions of 5 g. were taken, half being examined by the technique described by Young (1947) and half by the modification described above. Counting was facilitated by placing a sheet of paper with 1 cm. squares under the Petri dish. The results are shown in Table IV. The advantages of the modified technique were the increased numbers of trichinellae, their motility, and the absence of muscle fibres.

TABLE IV.—*Number of Trichinellae Found by Different Techniques*

Experiment No.	No. of Trichinellae/5 g. Tissue	
	Original Method	Modification
1	68	105
2	82	121
3	47	100
4	77	123
5	50	130
6	54	108
Total	378	687

The four specimens of diaphragm from pigs which were found positive gave the results shown in Table V.

The first 102 specimens of diaphragms from Pembrokeshire were examined histologically as well as by digestion, and in no instance were any trichinellae demonstrated, although one specimen (No. 87) was positive by the digestion technique. Owing to the limited material available it was unfortunate that an accurate comparison between the histological and digestion methods could not be made.

TABLE V.—*Number of Trichinellae Found by Different Techniques*

Specimen No.	No. of Trichinellae/5 g. Tissue	
	Original Method	Modification
87	4	9
108	17	25
131	27	51
173	3	10
Total	51	95

The three rats infected experimentally were apparently quite healthy when killed four weeks later. This experience would appear to differ from that quoted by Howell (1941).

Summary

The clinical and laboratory findings in an outbreak of trichiniasis affecting 25 persons in an area hitherto free from infection are described. The vehicle was found to be pork sausage-meat manufactured from a pig imported from one of two farms in Pembrokeshire. Pembrokeshire has been incriminated in earlier outbreaks in Wales, but on this occasion, for the first time, live trichinellae were demonstrated in rats and pigs from the suspected farms.

The clinical findings did not follow classical textbook accounts, but were similar to those described in recent years. Periorbital oedema as a presenting symptom is stressed in this outbreak. This, combined with eosinophilia developing within fourteen days, is in our opinion pathognomonic of trichiniasis. Muscle pains were almost always present, but gastro-enteritis occurred in only 16% of the cases.

In contrast with outbreaks in Germany and the U.S.A., no deaths occurred, though two persons were seriously ill. This is, in our view, due to a lower infecting dose from consumption of undercooked as opposed to raw sausage-meat.

A modified digestion technique for the demonstration of trichinellae in muscle is described. It makes use of both peptic and tryptic digestion of the muscle fibres and leaves the larvae still motile. Compared with Young's method, it revealed nearly twice as many larvae in rat muscle and in pig diaphragms.

We wish to thank Dr. J. Spillane and Dr. A. J. Thomas for permission to publish details of their cases; the general practitioners of Barry; Dr. Speedy, medical officer of Health, Western Districts of Pembrokeshire, and Dr. McKim Thomas, medical officer of health, Cardiff Rural District Council, and their sanitary inspectors; Professor Jethro Gough and his staff for histological and some haematological investigations; and Dr. Scott Thomson for his constant advice and encouragement.

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The results of experiments in the control of blowflies in North London railway sidings where refuse is collected and sorted is given in the report of the Pest Infestation Research Board for 1952, which was published recently. At the height of the season it was estimated that there were some 25,000,000 blowfly grubs in 15,000 sq. ft. of ground. A dust insecticide was found to be the most effective in their control, and D.D.T. was used twice weekly. In order to obtain information about the rate of dispersal of the flies the Laboratory fed them on a radioactive phosphorus salt and then released them from the refuse sorting depot. Traps were placed over a radius of two miles, and it was established that the flies covered a distance of at least a mile a day. Some of them were examined at the Central Public Health Laboratory, and all were found to be carrying food-poisoning organisms. The report is published for the Department of Scientific and Industrial Research by H.M. Stationery Office, price 2s.

THE BLOOD PRESSURE DURING CARDIAC MASSAGE IN MAN

BY

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Cardiac massage, by which is meant rhythmic manual compression of the heart, is an accepted part of the treatment of cardiac arrest and ventricular fibrillation occurring during anaesthesia or surgical operations. This measure has been justified by the reports of resumption of the heart beat, and less frequently survival, following its use, when the dysrhythmia has been prolonged. The explanation usually given of its beneficial effect is that the heart may respond to the local mechanical stimulus and also that the procedure is a means of maintaining the circulation.

In experiments on dogs cardiac compression between the fingers and thumb has maintained a cardiac output of approximately half that resulting from spontaneous activity under the conditions of the experiment (Johnson and Kirby, 1950). McMillan *et al.* (1952) have observed in dogs during cardiac massage a blood pressure of 40 mm. Hg. However, there are no reports of direct measurements on the circulation in man during cardiac massage, and there is consequent uncertainty of its effectiveness. The observations recorded here offer some information on this point.

We have been recording the intra-arterial blood pressure during certain surgical operations by means of an electrical condenser manometer and a thin plastic catheter introduced into a suitable peripheral artery (Peterson *et al.*, 1949). On two occasions while we have thus been recording the systemic blood pressure cardiac arrest has occurred and we have been able to record the effect of manual cardiac compression on the peripheral circulation. Both patients had severe heart disease (rheumatic aortic incompetence) with gross cardiac enlargement, and both were undergoing thoracotomy.

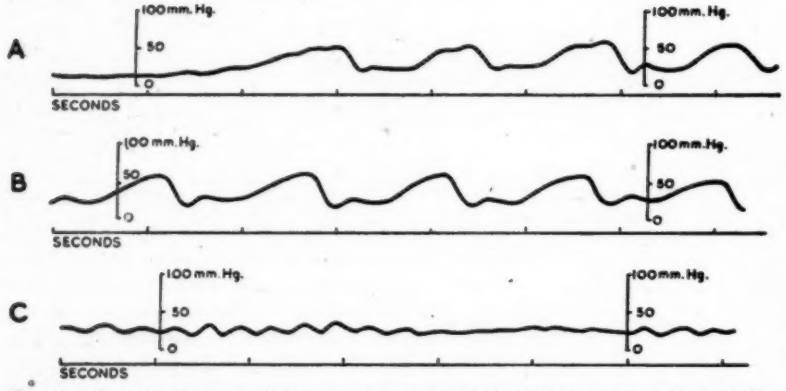

FIG. 1.—Case 1. Intra-arterial pressure records obtained during a period of cardiac arrest. (A) The record obtained when cardiac massage was started; (B) during cardiac massage. (C) Record obtained when cardiac massage was temporarily interrupted and there was thought to be ventricular fibrillation.

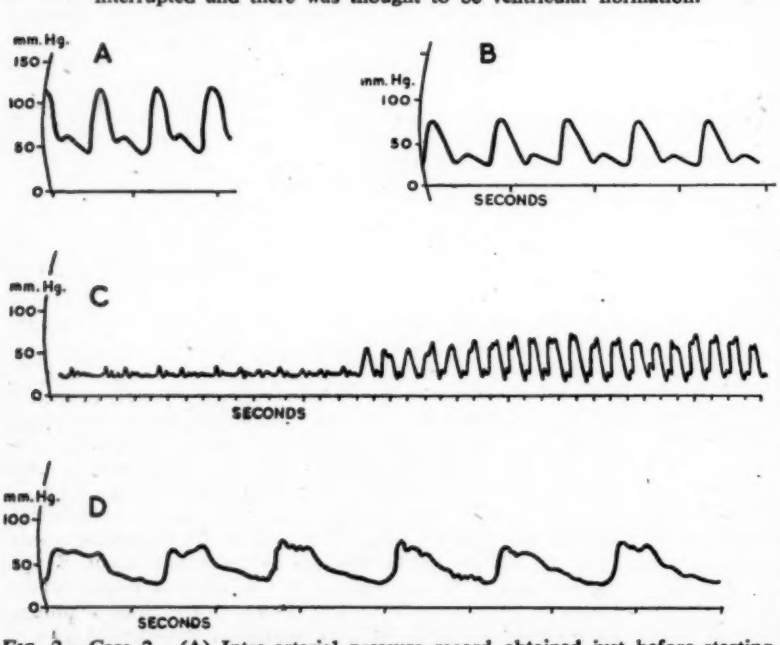

FIG. 2.—Case 2. (A) Intra-arterial pressure record obtained just before starting the operation. (B) Record obtained during course of operation before onset of cardiac arrest. (C) Record obtained during period of cardiac arrest just before and during beginning of cardiac massage. (Note slower paper speed.) (D) Record during cardiac massage showing slow-rising plateau form of pulse wave.

Case Reports

Case 1.—A man aged 50 had a blood pressure before operation of 220/110. It fell sharply during the induction of anaesthesia, and by the time the skin incision for a right thoracotomy was completed the systolic pressure was 100 mg. Hg. As the muscles of the chest wall were being incised the heart stopped. The chest was rapidly opened through the third intercostal space with division of the third costal cartilage, and 10 ml. of 1/10,000 solution of adrenaline was injected into the heart. Cardiac massage was begun with the pericardium intact. During this procedure the pulsations shown in Fig. 1, A and B, were recorded from the brachial artery. This pulsation coincided with the compression of the heart and ceased when it was interrupted. During one such interruption the record shown in Fig. 1, C, was obtained. The heart at this time was thought to exhibit ventricular fibrillation. The records are admittedly over-damped, but they show a sustained pulse wave of 55/20 mm. Hg at a rate of approximately 50 a minute.

Case 2.—A man aged 48 had a blood pressure of 140/35, measured by sphygmomanometer, before operation. The intra-arterial pressure just before the skin was incised was 120/40 (Fig. 2, A). During a long and difficult operation the pressure fell gradually to 75/25 (Fig. 2, B). Then in the course of a few minutes the blood pressure fell steadily to an insignificant level and the heart action became very weak. Cardiac massage with two hands encircling the very large heart was begun immediately, and produced a palpable pulse in the temporal arteries. Fig. 2, C, shows the brachial artery pulsations just before and at the beginning of cardiac massage. Fig. 2, D, is a tracing made at the same paper speed as Fig. 2, A and B, and shows the shape of the pulsation produced by cardiac massage. The peripheral blood pressure resulting from cardiac massage was about 70/30, with a maximum of 75/30, at a rate of approximately 50 beats a minute.

Discussion

Maintenance of the circulation during cardiac arrest (together with adequate administration of oxygen) is important for two reasons. A heart which is anoxic is unlikely to resume its normal rhythm and the dysrhythmia itself is often the result of anoxia. Anoxia from cessation of the circulation of more than three minutes' duration may be followed by irreversible damage to the central nervous system. Thus the question whether cardiac massage has a beneficial effect because it provides a local mechanical stimulus to the heart or because it is a means of maintaining the circulation is not an academic one. If it can be shown that it serves the latter purpose then its importance in this respect far outweighs the former, and the operator must not be content with merely gaining a limited access by which to apply some mechanical stimulus to the heart. His exposure must enable him to achieve as efficient a pumping action as possible.

Our tracings offer evidence that cardiac massage in man is an effective means of maintaining some peripheral circulation. In one case the peripheral blood pressure during this manœuvre was 75/30 and in the other it was 55/20 even with the pericardium closed. The blood pressure depends not only on the cardiac output but also on the peripheral resistance, so that the recording of such pressures does not provide an exact indication of the amount of the circulation. It is possible that over a short period of time intense peripheral vasoconstriction could result in such pressures being achieved with only a small cardiac output. But this consideration does not detract from the possible value of the procedure, for it is generally believed that such vasoconstriction does not involve the cerebral and coronary circulation, and is in fact a means of achieving a favourable distribution of blood to these organs. Thus it is reasonable to suppose that the recording of such pressures offers evidence that the flow of blood to the brain and heart achieved by cardiac massage is of considerable value. Reports of recovery without serious cerebral damage, following cardiac massage for several minutes (for example, Coyne, 1952; Touroff and Adelman, 1949), also support this supposition.

The shape and amplitude of the peripheral pulse depend on the volume, rapidity, and duration of cardiac ejection and the elasticity and state of contraction of the peripheral vessels. In both cases we recorded a slow rising and sustained pulse; this characteristic may be connected with the difficulty reported by others in detecting the pulse by palpation or auscultation and measuring the blood pressure by means of a sphygmomanometer (McMillan and Cockett, 1952).

Summary and Conclusions

In two cases a record of the peripheral pulse has been obtained by means of an intra-arterial catheter and an electronic manometer during the performance of cardiac massage. The records obtained offer evidence that cardiac massage is capable of maintaining some circulation. It follows that for cardiac massage to be properly performed the surgical approach must enable the heart to be firmly grasped.

We wish to thank Mr. R. C. Brock for his encouragement to prepare this report.

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DRUG RESISTANCE IN MALARIA

BY

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The resistance of many cases of malaria to drug treatment has long been a matter of concern to those who have to treat this disease, and so far no satisfactory solution has been found. The evidence submitted here suggests that infestation with hookworm, which is endemic in all malarious areas, or with other blood-sucking or blood-infesting worms, is a cause of malaria being resistant to drug treatment.

A chance observation in a very resistant case of malaria (*Plasmodium falciparum*) in which the parasites persisted in the blood in spite of repeated courses of treatment with proguanil, mepacrine (by intramuscular injection), and quinine, used either singly or in combination, showed that the patient was excreting hookworm in the faeces. It was observed that by the day following treatment of the patient for hookworm the malaria parasites, fever, and general symptoms had disappeared. During the next 8–9 months 12 similarly resistant cases were studied. All were shown to have hookworm infestation, and all failed to respond to antimalarial treatment until hookworm treatment was given, when they immediately responded.

In January, 1949, a large-scale study was begun. All cases of malaria were thenceforward treated for hookworm and observations made to see whether, compared with previous years, the relapse rate fell and continued at a low level. The standard of "relapse" adopted was that any case returning with malaria within six months of the original treatment was to be regarded as a relapse and not as a new infection, unless the parasite found was of a different variety from the previous one. The drugs and methods of treatment used were the same in all the years mentioned in Tables I and II, except that in 1948 hookworm treatment was not given.

TABLE I

	1948		1949		1950		1951	
	New Cases	Relapses	New Cases	Relapses	New Cases	Relapses	New Cases	Relapses
Plasmodium:								
Vivax ..	8	26	3	1	5	2	4	1
Malariae ..	94	217	94	24	14	6	65	7
Falciparum ..	219	712	127	37	70	9	307	44
Total ..	321	955	224	62	89	17	376	52
% relapses to new cases	297·5		27·7		19·1		13·86	

Results

Table I refers to proved cases of malaria in which parasites had been demonstrated. In Table II are presented the number of cases suspected of malaria clinically in which no parasites were found but other evidence—for example, malaria debris, monocytosis, etc.—was usually present. The results given in both tables show a great reduction in the malaria relapse rate and have a similar trend, though the relapse figures for 1950 in Table II are slightly higher than might be expected; this may be due to a period of four and a half months' leave, during which the diagnosis was in the hands of a locumtenent with rather less experience of malaria.

The figures for 1947 were in general similar to those for 1948.

TABLE II

	1948		1949		1950		1951	
	New Cases	Re-lapses	New Cases	Re-lapses	New Cases	Re-lapses	New Cases	Re-lapses
Cases of clinical malaria . .	472	1,302	1,175	429	1,465	977	1,486	175
% relapses to new cases	275·8		36·5		66·7		11·8	
No. attending at clinic	14,279		19,196		26,586		19,504	
No. of blood films examined . .	2,459		1,791		1,756		2,879	

Discussion

Hookworm has been especially mentioned, as it is believed to be the main cause, but whipworm has been present in most of the infested cases, and occasionally roundworm; tapeworm not at all. The hookworm infestation rate in this area is in the region of 80%.

When attached to the gut wall the hookworm is known to inject an anticoagulant into the blood stream to prevent clotting while obtaining blood. It is possible that either this anticoagulant or some other unknown substance injected at the same time has the effect of preventing the action of antimalarial drugs. It seems unlikely that the hookworm acts by absorbing the drugs while they are still in the intestine, because mepacrine and quinine when given by injection have also often failed to act until the hookworm treatment has been given.

It is possible that the hookworm treatment causes the hookworms to release their hold on the intestine, and their products may be destroyed or be eliminated from the body. The antimalarial drugs may then exert their effect before the surviving hookworms are able to regain their position and activity.

Medical Memorandum

Generalized Actinomycosis with Possible Cardiac Involvement

Actinomycosis is not uncommon in the classical sites, but general dissemination is infrequent and endocardial involvement rare. Cornell and Shookoff (1944) found only 18 reported cases with endocardial ulceration capable of causing pyaemia. In only two were valves infected; the remainder arose by direct spread from the mediastinum (11) or by embolic involvement of the myocardium (5). One of their personal cases, a clinical mitral lesion, violates any pre-mortem diagnosis of an actinomycotic valve infection: the valves were normal at necropsy, but granulation tissue had penetrated the auricle from the mediastinum.

Localized lesions usually yield *Actinomyces bovis*, a non-acid-fast anaerobe. The acid-fast aerobic organisms are pathologically less common, but more often cause generalized spread (Cope, 1938). Cases recently reported incriminate members of this group (Custis *et al.*, 1944; MacNeal *et al.*, 1946; Stokes *et al.*, 1951).

A case is reported below in which general dissemination was due to *A. bovis* of probable endocardial origin. Prolonged penicillin therapy resulted in apparent cure.

Case Report

An apprentice joiner aged 18 was admitted on December 20, 1950. Eight months previously he had a left facial palsy following an injury to the homolateral mastoid region, the site of mastoidectomy at the age of 6. Lassitude, weight loss, and stabbing pains deep to the xiphisternum on bending forward and local pressure then started. Three-day periods of discomfort in the same situation were accompanied by dyspnoea on exertion. Later, "cramps" in his calves on walking preceded the appearance of tender swellings.

Examination revealed a harsh aortic systolic murmur with a split second sound and accentuated pulmonary second sound. Discrete, tender, subcutaneous swellings 2 to 4 cm. in diameter were present in the calves and thighs—some fluctuant, others firm. The feet were plantar-flexed, and dorsiflexion caused pain. Knee movements were similarly limited. Diagnosis was not aided by numerous investigations. A blood culture yielded a spore-bearing organism rejected as a contaminant. An *x*-ray film of the chest showed equivocal opacities at the right base; the posterior mediastinum was seen to be clear. Biopsy revealed non-specific lymphocyte infiltration and fibroblastic reaction.

The temperature ranged from 98 to 100° F. (36.7 to 37.8° C.), and the pulse 100 to 110. Bacterial endocarditis (organism not known) was diagnosed and penicillin, 250,000 units four-hourly, was administered for seven weeks. The temperature settled in six days, but the tachycardia persisted until the sixth week, when the spleen was palpable for a few days. Pain, tenderness, and the abnormal heart sounds disappeared, though some nodules persisted. For the next six weeks he remained well, but new lesions developed on the legs and forearms.

In April, 1951, the patient was admitted to the Manchester Royal Infirmary. Both firm and fluctuant nodules were present on the arms and legs; the calves felt woody. There was no fever, splenomegaly, or cardiac abnormality. *A. bovis* was isolated from a fluctuant lesion, and microscopy of the faeces showed many morphologically similar organisms. An *x*-ray film of the chest remained equivocal. Penicillin ("distaquaine"), 600,000 units eight-hourly, was given for 16 days, and then once daily for two months. All lesions gradually subsided. In September, 1952, he was well; an *x*-ray film of the chest showed no change, and there were no actinomyces in the faeces.

Discussion

The varying cardiac bruits suggested the endocardium as the focus for pyaemic spread. Whether it was on the valves, or whether it was on the mural endocardium as described by Cornell and Shookoff, could not be decided. The lungs were an unlikely focus for dissemination. The faecal actinomyces and retrosternal pain indicated a primary oesophageal lesion, possibly spreading to involve the endocardium. The absence of mastoid inflammation made it an unlikely focus for a blood-borne endocardial infection. The fresh lesions after the disappearance of cardiac signs may have been due to the slow growth of deposits already in the tissues and not to the persistence of the cardiac focus.

Penicillin therapy should be prolonged in systemic actinomyces infections; with small dosage, up to nine months has been necessary (MacNeal *et al.*). Chloramphenicol, however, has proved successful after four weeks in an *Actinomyces muris* infection (Stokes *et al.*). The present case suggests that with the current large doses of penicillin at least three months' treatment is necessary, though one daily injection of a long-acting product may be enough after the first month.

Finally, in a case of doubtful pyaemia an unusual spore-bearing organism from blood culture should not be lightly disregarded as a contaminant.

Our thanks are due to Professor T. H. Oliver for his kind co-operation and to the Department of Clinical Pathology, Manchester Royal Infirmary.

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Reviews

HISTOCHEMISTRY

Histochemistry: Theoretical and Applied. By A. G. Everson Pearse, M.A., M.D., D.C.P. (Pp. 530; 4 coloured plates and 109 black-and-white illustrations. £3) London: J. and A. Churchill. 1953.

This book is an outstanding contribution to the literature of a relatively new, rapidly growing, and supremely important branch of biology. The purpose of histochemistry is to submit a tissue section to chemical analysis while at the same time preserving the details of its minute structure. Not only are chemical substances identified in the section but their nuclear, cytoplasmic, or extracellular location can be accurately defined, and there is every justification for the author's statement that "histochemistry can transform the descriptive sciences of biology, histology, pathology, and zoology into dynamic and functional sciences complementary to physiology and biochemistry."

The book is designed "to compass the whole of histochemistry, as applied to tissue sections," and deals "solely with the theoretical and practical aspects of microscopical histochemistry." Until its publication there was no modern treatise available which correlated the numerous and often complex chemical and histological techniques of the subject with the chemical theory on which they are based. Without such correlation progress in histochemistry is likely to be retarded and the subject to become a rigid and empirical technology. The author has discussed the technological aspect of his subject in a very sensible way. He does not confuse his account of chemical theory with technical minutiae. These are collected together at the end of the book as a series of appendices to each chapter, and this practical part of the book is all the more valuable because the author has personally tested out all available methods, modifying some of them and rejecting others as useless.

The chapters dealing with theory are clearly written. An account of the chemistry of fixation is followed by another on the preparation of tissues by freeze-drying. A valuable section, occupying six chapters and about a third of the book, is on the recognition of many of the biochemical constituents of tissue sections. About a quarter of the text is on the identification of enzymes, and there are shorter chapters on pigments, inorganic tissue constituents, and the use of physical methods.

The author quite clearly shows what histochemistry has to offer as a scientific discipline, but does not neglect to emphasize its defects and difficulties. Once its vast possibilities are appreciated it must be agreed that the author is justified when he says, "All those whose occupation is with tissue sections . . . must become applied histochemists if the science is to realize its fullest capabilities."

GEOFFREY HADFIELD.

RESULTS OF ARTIFICIAL PNEUMOTHORAX

Brompton Hospital Reports: A Collection of Papers Recently Published from the Hospital. Volume 21, 1952. (Pp. 206; illustrated. 15s.) Copies may be obtained from the Secretary, Brompton Hospital, London, S.W.3.

The Brompton Hospital Reports are looked forward to by those interested in tuberculosis and diseases of the chest with justifiable eagerness and enthusiasm. Usually the volume is a collection of papers by members of the medical and surgical staff that have been published during the year. In the present issue this practice has been followed, but, in addition, half of the volume is taken up by a special report on the results of collapse and conservative therapy in pulmonary tuberculosis. This contribution makes the 1952 *Reports* of particular value at the present time, when the value of artificial pneumothorax treatment is being contested by many and has already been given up altogether by some chest physicians. This special report is supported by an article by the same authors on artificial pneumothorax which appeared in the *Quarterly Journal of Medicine* (1951, **20**, 313), and the remaining part of the volume is taken up by previously published papers on chemotherapy, diagnosis, bronchiectasis, and bronchography.

The investigation on collapse therapy was carried out on 1,153 patients who were discharged from sanatoria during the period 1937 to 1942, which allowed for a minimum period of observation of eight years. In the series, 955 of the patients had cavitated disease and 198 had no cavitation. These two groups were further subdivided into 644 patients with cavitated disease, who had some form of collapse therapy as an initial measure, and the remaining 311, who were given routine sanatorium treatment only. The 198 patients without obvious cavitation were followed for 8 years; 130 of these had rest and sanatorium treatment; 68 had collapse therapy, of whom 62 had unilateral pneumothoraces. Of the 1,153 patients, only 13 (1.13%) were lost from observation.

The investigation set out to determine statistically the difference between the fate of patients who had cavitated disease and were treated by collapse therapy and those who were not so treated, and also to find out what was the effect of anatomically perfect and imperfect collapse on the prognosis of patients who were given pneumothorax treatment. In order to achieve this aim, careful assessment of the extent of the disease, size of cavitation, and presence or absence of tubercle bacilli in the sputum had to be performed in each case throughout the period of observation. This was done in all cases, and the results have been clearly tabulated, discussed, and summarized.

The main findings confirm the conclusions that have been made by previous surveys, which are summarized in one section of the report. But there are some that have not been proved previously and which are of importance at present.

Of the 311 patients who had no initial collapse therapy, 256 had no active treatment at any time, and their chance of living five years was 58.6% and eight years 46.4%. 644 patients received similar treatment to the 311, except that some form of collapse therapy was instituted on their first admission to hospital. This was unilateral pneumothorax in 71%, thoracoplasty in 12%, and by other methods in 17%. Of all these patients, 66.5% survived for eight years. In patients with disease of the same extent there appeared to be no difference in prognosis if the disease was unilateral or bilateral, and collapse therapy did not materially improve the prognosis of patients in any class who had a persistently negative sputum.

The report analyses in detail the 457 patients treated with unilateral pneumothorax and the 77 patients treated with thoracoplasty, and then proceeds to the results of treating 198 patients without demonstrable cavitation as judged by ordinary *x*-ray films. Of these patients, 68 had collapse therapy as an initial measure and the remainder were treated by rest and sanatorium routine only. One of the conclusions that is perhaps rather surprising is that the results of thoracoplasty were statistically inferior to those of an adherent satisfactory pneumothorax.

The comparison between the different groups in the series is very wisely not pushed too far, and the reader is left a good deal of freedom to draw his own conclusions. There would seem to be no doubt that the majority who study this excellent piece of work will agree that it shows that pneumothorax treatment is of value in the selected case and can give very good results. The report also reminds us that 72% of patients with active lesions without demonstrable cavitation, treated by routine sanatorium treatment alone, showed no relapse during the eight years of observation and that in similar cases treated by artificial pneumothorax 87% were on full-time employment at the end of the eight-year period. (It would be an injustice and a waste of time and labour to submit this class of patients to major thoracic surgery, particularly when it is remembered that the report refers to cases treated in the pre-streptomycin era. Even better results may be expected with the combination of

collapse therapy and antibiotics). The valuable observations in this article show how necessary it is to exercise the greatest care in selecting patients for major thoracic surgery, which has its rightful place in treatment but must not be abused in the same way as artificial pneumothorax treatment was almost indiscriminately applied in the past and therefore fell into disrepute. It is equally important that patients should not be submitted to surgical procedures if they can recover without them.

This is supported by the results obtained by Scadding and Nicholson; they are set out in the next paper in the *Reports*. Here is given the experience of the careful treatment of 50 patients with artificial pneumothorax over a period of fifteen years. Thirty-eight of the original patients are well and working, six have died from tuberculosis, one died from an unrelated illness, and five are in relapse. The complications are discussed, and the authors stress the need for a single control policy throughout treatment.

The remaining sixty pages of the volume are occupied by reprints which are all of practical value, in particular those on radiography. A technique for producing bronchograms in children with the aid of general anaesthesia is described, and there is a clear and helpful paper on the radiological appearances of primary tuberculosis in children with a number of good *x*-ray pictures illustrating the differential diagnosis.

FREDERICK HEAP.

DISEASES OF THE OESOPHAGUS

Diseases of the Esophagus. By Philip Thorek, M.D., F.A.C.S., F.I.C.S. (Pp. 140. 102 illustrations. £4.) Philadelphia, London, and Montreal: J. B. Lippincott Company. 1952.

From the surgeon's point of view this book deals with diseases of the oesophagus more than adequately. The chapters cover anatomy, embryology, physiology, methods of examination, general surgical considerations including approach and technique, and the various lesions, congenital and acquired, for which surgery may be undertaken. The illustrations, whether of unusual conditions such as the abnormalities of the aortic arch that may cause oesophageal obstruction, or of operative technique, are admirable. Fig. 92 suggests an unduly conservative resection for cancer at the cardia; Figs. 49 and 50 illustrate forms of oesophagogastrostomy that have been abandoned in Britain; and Fig. 100 shows transplantation of the oesophagus to get it out of the way of a big heart, an operation in the true Heath Robinson tradition. But these figures illustrate the author's wish to cover all aspects of the subject rather than his personal recommendations. These, as given in the text, are sound and clearly stated. A surgeon seeking up-to-date information, or a lecturer seeking illustrations, will find them in this book.

HENEAGE OGILVIE.

PSYCHIATRY AND CRIME

Psychological Disorder and Crime. By W. L. Neustatter, M.B., M.R.C.P. Foreword by John Maude, Q.C. (Pp. 248. 21s.) London: Christopher Johnson. 1953.

The Psychopathic Delinquent and Criminal. By George N. Thompson, M.D., F.A.C.P. (Pp. 157; illustrated. £1 12s. 6d.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1953.

The importance of psychiatric concepts for an understanding of the mind of the criminal and the causes of crime is being gradually brought home to the legal fraternity and to the general public. Any contribution to this useful end that medical men can make is very much to be encouraged. The evidence that psychiatry can provide is certainly more realistic and more relevant now than it used to be, and every year sees a growth in these respects. The two volumes for review both represent an attempt to explain in simple language what this evidence may be.

Dr. Neustatter's book is addressed to the non-medical world, to lawyers, probation officers, social workers, administrators, etc. He remarks in his preface, "I have never understood why a fascinating subject like psychiatry cannot be presented factually to the layman—as biology and astronomy are." This sentence provides the key-note of the work, and is more than sufficient explanation and excuse for many passages which a medical man, let alone a psychiatrist, would be inclined to criticize as superficial or oversimplified. We have to recognize that the legal stomach for unfamiliar ideas is excessively queasy, and that anything of this kind that is provided has to be in an easily digested pap. Dr. Neustatter's kindness and thoughtfulness are beyond reproach, and he refrains from exciting antagonism by committing such a *faux pas* as an attack on the M'Naghten Rules. Every psychiatrist who has ever had to meet a legal confrère will wish Dr. Neustatter's bold venture well.

Professor Thompson's book comes from the U.S.A. and is rather more technical. The field covered is also a more restricted one, that of the psychopathic criminal, and in successive chapters he briefly considers terminology, aetiology, pathology and psychopathology, course, and treatment. The handling of the subject, though intended for a medical audience, is somewhat scrappy and superficial, and the amount of space which, in a rather short book, is given to clinical histories seems excessive. The section on electroencephalographic research, for instance, is entirely inadequate, and the author appears to be ignorant of the important work that has been done by Denis Hill and his co-workers. As it is, the book falls between two stools, being rather technical for the non-psychiatric reader and insufficiently scholarly for the psychiatrist. However, it does serve the author's good intentions, of promoting the diagnosis and treatment of the mentally abnormal criminal instead of his uncomprehending punishment.

ELIOT SLATER.

GOUT

Gout and Gouty Arthritis. By Professor John H. Talbot, M.D. Modern Medical Monographs, 7. (Pp. 92; illustrated. $4.) New York: Grune and Stratton. 1953.

An understanding of gout, as opposed to its recognition, is still far from complete. Professor Talbot has set out to describe the significant advances in elucidation of this age-old problem. It follows, therefore, that it is the biochemical and physiological approach which receives the greatest emphasis. Of the various possible causes of the rise in circulatory urate in the gouty person, he favours increased formation of endogenous uric acid due to enhanced metabolism of the purines. This leads to an interesting study of isotopes in respect of purine metabolism. He discusses the mode of action of salicylates and probenicid, and clearly defines the use of colchicine. It is interesting to note that the author finds colchicum quite as effective as cortisone in acute gout.

The section on *x*-ray diagnosis is unnecessarily long, while those on diagnosis and differential diagnosis should either be greatly extended or deleted. As it is, they fail to provide the all-important clinical picture.

A. H. DOUTHWAITE.

OSTEOSCLEROSIS

Osteosklerose und Knochenmarkfibrose. By Rudolf Stodtmeister, S. Sandkühler, and A. Laur. (Pp. 134; M. 11.) Stuttgart: Georg Thieme. 1953.

This is a monograph from the medical school of Heidelberg on the somewhat rare but important diseases in which sclerosis of the bones and fibrosis of the medulla are the primary features. The study here presented was based on a series of 23 cases and a thorough review of the literature. The cases have been investigated in most elaborate detail, and are admirably presented. Radiographs, both clinical and pathological, and coloured blood films help to clarify the full description of complex pathological conditions. The whole forms an impressive account of a difficult subject and should be of real value to the specialist.

HENRY SOUTTAR.

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THE PRESIDENT'S ADDRESS

Mr. J. W. Tudor Thomas is the sixth ophthalmologist who has held the high office of President of the British Medical Association, and in the admirable Presidential address he delivered at Cardiff on Monday, and published in our opening pages, he showed that his specialty has not narrowed his vision of the medical scene. This year's meeting in Wales is historic because it marks the jubilee of the Representative Meeting, which was first held in Swansea in 1903. And it was just a hundred years ago that the B.M.A. celebrated its twenty-first birthday at the first annual meeting to be held in Wales. Mr. Tudor Thomas has therefore aptly seized the occasion for a historical survey which puts the present in the setting of the past and reminds us of the many notable parts played by our forebears in medicine. By the happy choice of a phrase from the address given in 1832 by the founder of the Association, Charles Hastings, Mr. Tudor Thomas underlines the motives that have always guided the good doctor in his work, and points to the inspiration that lay behind the establishment of the Provincial Medical and Surgical Association which in 1856 changed its title to the one it has now borne for ninety-seven years. In these days, when the B.M.A. is by force of circumstances so largely preoccupied with medico-political problems, it is salutary to be reminded by the President that the founder of the B.M.A. put as the first object of association "the diffusion and increase of medical knowledge in every department of science and practice." And he enjoined his colleagues to further this "with head, and heart, and hand." Mr. Tudor Thomas reminds us, too, that the remarkable man who founded the Association started a quarterly journal in 1828 called the *Midland Medical and Surgical Reporter and Topographical and Statistical Journal*. The choice of this title shows astonishing prescience of the problems facing medicine, and Mr. Tudor Thomas does well to point out that in the original prospectus of the Association Hastings clearly saw the importance of preventive medicine and occupational health. He was a man of vision, and the vision must be kept bright.

With a true sense of the continuity of history Mr. Tudor Thomas took his audience on Monday for a short journey back into the centuries before 1832. The familiar tale is always worth retelling so that medical men and women may be reminded that the foundations of the art and the science were laboriously laid by men of genius often working with little else but their unaided senses and sharp minds. It is perhaps difficult to-day to realize the extent to which the senses have, so to say, been amplified by the invention of ingenious instruments. When the Association was founded at the beginning of the last century Laennec introduced the stethoscope, now the traditional hall-mark of the clinician. As Mr. Tudor Thomas tells us, there was then no laryngoscope, no ophthalmoscope, and not even the clinical thermometer. The hypodermic syringe was yet unthought of. When Charles Hastings began practising he had to do his work without those instruments now regarded as an indispensable part of the practitioner's equipment, without which, indeed, the modern doctor would feel completely lost. Yet amid all the clutter of instruments and facts from the laboratory the practitioner to-day can still with profit go back to Hastings for guidance. He stressed the need for gathering information by direct observation, for correlating the observed facts with the habits and occupations of patients, with variations in climate and soil. His vision of the practical problems of medicine was probably all the sharper for the lack of many adventitious aids, and if we boast to-day of the large membership of the Association we should not forget those 300 or so men who shared Hastings's vision in 1832 by joining with him in the active promotion of "medical knowledge in every department of science and practice."

Mr. Tudor Thomas, Hastings's successor to-day, has in his own work carried his predecessor's precepts into practice, and has extended knowledge in his own "department of science" by his notable contributions on corneal grafting. Ophthalmology is probably the oldest specialty in medicine, and has attracted many brilliant men to its study, not least among them this year's President of the B.M.A. The progress in ophthalmology since the introduction of the ophthalmoscope by von Helmholtz in 1851 has been as rapid as in other branches of medicine. The ophthalmologist, too, has made contributions of first importance to physiology and general medicine, and perhaps more than any other specialist has to keep abreast with work done in many other fields of research. Mr. Tudor Thomas's interesting observations on medical literature are a reflection of this, and many will echo his plea for more leisure for the medical man so that he may have time to read and to digest what he has read. Those many who will read the Presidential address in this week's *Journal* will,

we may be sure, find in it much to reflect upon, many new trains of thought to follow, and an inspiration to look at their own work in a fresh and invigorating light.

CLINICAL RESEARCH IN THE N.H.S.

Medical research is the life-blood of medical practice, and plans published this week for greatly developing the means of conducting it in Britain deserve the warmest welcome. Under the National Health Service Act, 1946, the Minister of Health was empowered to undertake research or to help others to do so. Up to now there have been no clear ways or means of exercising these powers, and to get the issues clarified a joint committee of the Medical Research Council and the Standing Medical Advisory Committee of the Ministry of Health was set up in 1951 under the chairmanship of Sir Henry Cohen. The joint committee's recommendations, now accepted in principle by the Ministers concerned, are published in a White Paper.[1] In essence the recommendations, which are printed in summary form on page 147, are as follows. A central organization called the "Clinical Research Board" is to be set up jointly by the Medical Research Council and the Health Departments (the Ministry of Health and Department of Health for Scotland), and it will be responsible for promoting clinical research on a national basis. The Board, which will be a small one with about ten members, will be established as part of the Medical Research Council and administered separately from the Health Departments. In coming to this decision the joint committee had in mind the considerations which led to the establishment of a separate Medical Research Council. The employing and financial authority for centrally organized clinical research will be the Medical Research Council, which already spends £431,500 annually on clinical research projects. It is suggested that additional funds should be made available to the Clinical Research Board, rising from £50,000 annually at first to £250,000 in three or four years' time. The joint committee emphasizes that it is a prerequisite of its recommendations that additional funds should be provided for the Board. After the new Board has been set up encouragement is to be given to "decentralized research supported by Exchequer funds at the level of boards of governors, regional hospital boards, and hospital management committees." The allocation of research grants to regional hospital boards may depend to some extent on the amount of endowment moneys available locally. If the research organization is to work well there must be effective machinery for consultation at all levels, and provision is to be made for this. Careers in clinical research will be equated in all material respects with careers in the National Health Service. Senior clinical research workers should have the full status of consultants or specialists and be entitled to the same distinction awards. Senior appointments will be made by the Medical Research Council, but regional hospital boards will be able to appoint clinical research workers up to senior registrar level. Research units will not be imposed on hospitals, nor clinical research workers promoted to senior posts without the agreement of the hospitals concerned, and it is hoped that regional and hospital authorities will seek the advice and help of the Clinical Research Board about their own research projects.

The medical profession will give the warmest welcome to this laudable scheme, which will help to raise standards of clinical work throughout the country. The status of the senior clinical investigator is put on the highest level, and this provision should attract some of our best intellects. Research into the mechanisms and causation of disease demands skill in clinical medicine. It cannot be done by hirelings who have to seek permission from above at every step and whose judgment of the patient's reactions could be vitiated by lack of appreciation of significant clinical detail. Clinical research ranges from the making of observations which are incidental to, and inseparable from, good practice to systematic investigations undertaken deliberately and often over long periods with the object of answering specific questions. The methodology of clinical research is as varied as the range of the sciences on which medicine is based, and the clinical investigator may use the techniques of any of them. The application of modern statistics to ordinary clinical and therapeutic data constitutes one approach. At the other end of the scale we see as the most modern development the application of human physiological research at the bedside. Human physiology was essentially begun by Haldane, who worked out the physiology of respiration in a uniquely beautiful and magnificently conceived fashion by experiment on himself and his colleagues. The application of comparable techniques to sick human beings at the bedside began with James Mackenzie and was extended by his pupil, Lewis. Their example started an era of research which has not yet reached its zenith but which has already led to great advances in the understanding of disease. Modern analyses of mechanisms in pernicious anaemia and heart failure are examples of this type of approach. Planned clinical research

[1] *Clinical Research in Relation to the National Health Service*, 1953, H.M.S.O., London.
[2] Report of the Medical Research Council for 1951–2, H.M.S.O.

is as vital to medicine to-day as post-mortem analysis of disease syndromes was in the last century. The extension of laboratory methods may sometimes make further detailed differentiation of disease pictures possible—for instance, in the haemolytic anaemias—but more often it puts a quantitative measure of the degree of disability into our hands. Among the other good results attained are a more logical basis for treatment and a sharpening of bedside diagnostic finesse, for instrumental methods often compel attention to the significance of finer physical signs formerly ignored because their meaning was debatable and understanding impossible.

We should feel content that these and similar applications of accurate observation, measurement, and experiment begun by our great predecessors from Harvey to Haldane are to be fostered and nurtured in these strenuous days. The annual report[2] of the Medical Research Council for 1952, published earlier this week, contains a most illuminating discussion of the reasons why clinical research is now at a stage when great progress can be expected and why organizational changes are necessary. The Medical Research Council, with its allied Clinical Research Board, may be expected to administer its resources with wisdom and integrity. The present powerful position of medical science stems completely from the development of scientific method. We may also be assured that invention and experiment will be applied to the problems of sickness in man with the humane spirit of perpetual and deep concern for his welfare that has characterized our profession down the ages.

THE JUBILEE A.R.M.

On July 28, 1903, the first Annual Representative Meeting of the British Medical Association was held after what Dr. Alfred Cox has described as a revolution in the constitution of the Association. That meeting was held in Swansea, and on Monday last in another Welsh city the Jubilee A.R.M. came to a successful conclusion. Certainly no more friendly and generous town than Cardiff could have been chosen for the occasion. In 1903 one of the first items of business was to elect a royal prince, later to become King George V, to honorary membership of the Association. Fifty years later in Cardiff the Representatives had the pleasure and privilege of electing to honorary membership another royal prince, this time the Duke of Edinburgh, who with the Queen was in Cardiff at the beginning of the Coronation visit to Wales on July 9. At an official reception in the City Hall Dr. P. T. O'Farrell, President of the B.M.A. for 1952–3, and Mr. Tudor Thomas, President for 1953–4, were both presented to the Queen.

The story of the events which led up to the first A.R.M. have often been told, but never better than by Dr. Alfred Cox,[1] one of the five surviving Representatives who attended the Swansea meeting. From Cardiff this year a telegram of good wishes was sent to each of these five—Dr. Cox, Dr. R. L. Langdon-Down, Dr. F. R. Hill, Dr. R. R. O'Brien, and Dr. W. St. A. St. John. The work of the early reformers has brought increasing credit to the Association, for, as Dr. Cox has said, "not only has it (the Representative Meeting) performed its function as the policy-making body of the B.M.A., but it has made itself into the nearest possible approach to a parliament of the medical profession." As with all parliaments, the importance of the matters discussed varies with the urgency of the occasion, and no doubt parts of the report of this year's meeting will seem as strange to Representatives attending the centenary meeting in 2003 as some of the debates at past A.R.M.s seem to us to-day. But Representatives at future meetings will not lack inspiration from the past. In this jubilee year of constitution-making we have already paid tribute in these columns[2] to the work of Victor Horsley, Alfred Cox, and James Smith Whitaker. Horsley was elected the first chairman of the A.R.M., and it was he who said, when he retired from office in 1906, that as a result of the revolutionary changes in its constitution the Association had proved its right "to take a part in the socio-political life of the Empire." Subsequent events have demonstrated the close relationship between medical and social progress and have underlined the wisdom of the founders of the A.R.M.

SEASICKNESS REMEDIES

The prevention of seasickness is a subject which arouses violent controversy, and it might sometimes be thought that we had made little progress. In fact knowledge has advanced greatly since 1939. At that time "mothersill" was still sold, a preparation relying on chlorbutol for its action; it is no longer discussed. Mixtures of atropine and hyoscine were also sold; they are no longer considered better than hyoscine alone. The controversy to-day is whether hyoscine (which is sold as "kwells") is more effective than one of the antihistamines, of which the favourites are promethazine ("phenergan") and diphenhydramine ("benadryl"). The last two are combined with chlorotheophylline to entitle them to the names "avomine" and "dramamine" respectively. This particular debate is a relatively tranquil affair, since there is no doubt that all the three rivals are useful agents, and that whoever takes one of them will be protected to a greater or less extent.

When so many experimental comparisons have been made it may seem surprising that the controversy persists at all. Can it not be stated once and for all which is the best? The answer is that this cannot be done without reference to the dose used. Glaser and Hervey[3] showed that 1 mg. of hyoscine hydrobromide protected a greater percentage of people than 25 mg. of promethazine or 25 mg. of diphenhydramine, promethazine being better than diphenhydramine. Their evidence was clear. But the usual maximum dose of hyoscine is only 0.5 mg., and their results do not tell us how much protection this

1 *British Medical Journal Supplement*, 1953, 1, 145.
2 Ibid., 1953, 1, 923.
3 *Lancet*, 1951, 2, 749.
4 *Brit. J. Pharmacol.*, 1953, 8, 187.

smaller dose would give. What is needed is an experiment which will tell us what doses of hyoscine, promethazine, and diphenhydramine afford protection to the same percentage of people. This can be done by determining the percentage protected by two (or three) doses of each substance. We can then proceed to examine the side-effects of the equivalent doses of the three substances, and we should be able to state that the best remedy was the substance which caused the fewest.

Glaser[4] has recently studied the side-effects of these substances using the doses chosen by Glaser and Hervey mentioned above. He states that all caused drowsiness and fatigue in a significant number of subjects, while other symptoms were proportionate to the effectiveness of these drugs against seasickness. There is an obvious dilemma here both for the doctor prescribing for seasickness and for the manufacturer choosing the dose to recommend on his preparation. If he chooses a high dose which will protect nearly all persons who take it, he will cause unpleasant side-effects in many who would have been protected by a smaller dose; while if he chooses a lower dose, which will cause fewer side-effects, an appreciable percentage of people will not be protected. Glaser confirmed that diphenhydramine has a very short action, while promethazine remains effective for a long time.

The question is sometimes raised whether these drugs can be taken daily on a long voyage. The answer would seem to be that they can. Hyoscine has long been used in the daily treatment of Parkinson's disease, and the antihistamines are used daily in chronic urticaria. Even so, most people feel better without such treatment, and clearly they should be used only when necessary.

AUTO-ANTIBODIES IN ACQUIRED HAEMOLYTIC ANAEMIA

Since the early years of the century it has been known that certain people suffering from acquired haemolytic anaemia possess "auto"-antibodies in their serum: these are antibodies which can be shown to react *in vitro* with the patient's own red cells. Early in 1946 the anti-human globulin test was used to demonstrate in a direct way that antibody globulin was indeed fixed to the red cells of most of these patients and, moreover, that it was fixed *in vivo*. The antibody thus demonstrated was thought to be "non-specific," that is to say directed against some hypothetical antigen possessed by all human red cells indifferently. A new phase in the study of the disease is opened by the case described in this issue of the *Journal* by Dr. W. Weiner and his colleagues. A man, after much illness, acquired haemolytic anaemia. His red cells were agglutinated by anti-human globulin, showing that antibody was fixed to them. Antibody could be separated from the patient's washed cells by elution: on investigation it gave the reactions of the well-known Rh antibody anti-e. Weak anti-e could also be detected free in the patient's serum, taken before his first transfusion. The patient is of the genotype CDe/CDe, so his red cells possess the antigen against which his serum contains the antibody.

With the exception of the familiar example of the transient passive transfer of antibody from mother into emybryo and from donor into recipient, this is the first clear demonstration of the presence of an identifiable antibody in a circulation which at the same time contains the corresponding antigen. It would be easy to mistake anti-e for a "non-specific" antibody, since it reacts with 98% of samples of blood, but now that it has been found as an auto-antibody in the serum of one patient suffering from acquired haemolytic anaemia it is likely to be found in others. There had previously been hints that "non-specific" antibodies might in truth be specific. The clear case reported in this issue makes it probable that many such will be found when the appropriate sera are investigated with the skill shown by the Birmingham team.

THE SEX RATIO AT BIRTH

That more boys than girls are born is a well-known and apparently permanent feature of human reproduction. But, in spite of much speculation, no wholly satisfactory explanation of it has yet been advanced. The sex ratio of live births is usually expressed as the number of boys per 1,000 girls born in a particular time and place. In England and Wales in 1951, the latest year for which figures are available, the ratio was 1,060. It is affected by social upheavals, and an increase in the proportion of boys born, with a consequent rise in the sex ratio, was associated with both the recent wars. The sex ratios at birth in England and Wales during the five years 1942–6 were the largest for the 109 years for which births had been recorded. Martin[1] suggested that the change was not solely due to the relative youth of the mothers giving birth, which was a feature of the war, but that the first-born children of mothers of all ages formed a larger proportion of all births than in peacetime and the first-born had a higher sex ratio than the latter-born children. Births in England and Wales have not been tabulated in a suitable form to show the sex ratio both by birth order and by age of mother—a defect in the data remarked on by Lowe and McKeown.[2] These authors found that the sex ratio for live births decreased with maternal age, while the sex ratio of the stillbirths increased.

Some new work on the subject has now come from MacMahon and Pugh[3] and Novitski.[4] Both these studies are of recent American data. MacMahon and Pugh show for white births that the sex ratio of live births decreases both with increasing birth rank and with increasing maternal age. But no consistent association with maternal age is found when the effect of birth rank is discounted, while a downward trend with birth rank remains in each maternal age group. Novitski found by the method of multiple regression equation, ignoring birth order, that the age of mother was not related to the sex ratio at birth but there was an association with age of father. Russell[5] in his

1 *Med. Offr*, 1948, **79**, 153.
2 *Brit. J. soc. Med.*, 1950, **4**, 75.
3 Ibid., 1953, **7**, 83.
4 *Science*, 1953, **117**, 531.
5 *J. Hyg. (Lond.)*, 1936, **36**, 381.

detailed study of the sex ratio at birth included American data, and he found for these that the ratio was highest among first-born children and declined with increasing size of family; there was little evidence of association with parents' age, but any relationship that might exist was with the age of the father rather than of the mother. Russell also showed that the ratio declined with descent in social class in England and Wales. He attributed this to the fact that in the higher social classes the families were smaller than in the lower classes, and consequently the first ranks of birth, with the highest sex ratio, were proportionately more important in the higher social classes.

From our present knowledge it would appear that variations in the sex ratio at birth are due to variations in the composition of the birth orders forming the population. This hypothesis gives a reasonable explanation of the large fluctuations observed during the war periods. Age of mother is, apparently, not a factor of any importance; whether the age of father is cannot yet be established because of the lack of suitable data.

JAUNDICE DUE TO METHYLTESTOSTERONE THERAPY

Methyltestosterone was introduced into clinical practice by Foss[1] in 1939, and because of its effectiveness when absorbed through the mucous membrane of the mouth it has become more and more generally used. Its efficacy has been established not only for androgen replacement therapy but also for many conditions in which the encouragement of protein anabolism is desirable. The first suggestion that it might be the cause of jaundice was made by Werner[2] in 1947, and in the following year Kinsell[3] also noticed an apparent relationship between icterus and the administration of methyltestosterone. In 1950 a report from the Columbia University Medical Center[4] confirmed earlier suspicions; seven cases of jaundice in which this androgen was convincingly implicated as the cause were described. Now Wood[5] has described another case and states that a number of similar cases have been observed at various clinics.

Wood's patient was a man of 32 who had been diagnosed as a case of idiopathic hypopituitarism and had received intermittent methyltestosterone therapy for two years; he had taken 20 mg. daily—a moderate dose—for the two months before admission to hospital with jaundice. On admission he complained of having had abdominal cramps and anorexia in the previous two weeks. The results of serial liver function tests showed marked and protracted hyperbilirubinaemia without a corresponding rise of the serum alkaline phosphatase. The cholesterol esters were depressed, but the values for serum protein fractions, thymol turbidity, thymol flocculation, and cephalin cholesterol flocculation were within normal limits. These findings, it is stated, are typical for methyltestosterone jaundice. Liver biopsy showed plugging of the intercellular bile canaliculi with bile pigment, but no evidence of inflammatory reaction, bile duct proliferation, parenchymal cell necrosis, or recent regeneration. Some three weeks elapsed after stopping methyltestosterone administration before the patient's symptoms disappeared; the jaundice itself cleared still more slowly.

The pathogenesis of the condition is obscure. Jaundice has not been reported after testosterone treatment; since this preparation, unlike methyltestosterone, does not cause creatinuria, the icterogenic effect of the methyl compound may be in some way associated with creatine metabolism. Another possibility is that an intermediate metabolite, rather than methyltestosterone itself, is the icterogenic agent, for we know that methyltestosterone, unlike testosterone, does not increase the 17-ketosteroid excretion and therefore must follow a different metabolic path.

Although there seems to be good reason to call attention to this hitherto generally unsuspected cause of jaundice, it is doubtful if the existence of liver disease, even with jaundice, should be regarded as a contra-indication to treatment with methyltestosterone in those conditions where it is indicated. Indeed, Lloyd-Thomas and Sherlock[6] have recently shown that it relieves the distressing pruritus of obstructive jaundice. They found that, though it increased the depth of jaundice, it was quite harmless, apart from its well-known masculinizing tendencies in women.

1 *British Medical Journal*, 1939, **2**, 11.
2 *Amer. J. Med.*, 1947, **3**, 52.
3 *Gastroenterology*, 1948, **11**, 672.
4 Werner, S. C., *et al.*, *Amer. J. Med.*, 1950, **8**, 325.
5 *J. Amer. med. Ass.*, 1952, **150**, 1484.
6 *British Medical Journal*, 1952, **2**, 1289.

PREVENTION OF HEPATITIS

The dangers of transmitting serum hepatitis to patients from blood and its constituents are not sufficiently borne in mind. Whole blood, serum, plasma, and other fractions are too often administered to patients for whom the probable benefit does not justify the risk. Hepatitis is an increasingly important problem, and a recent report by a W.H.O. committee[1] will be useful to doctors seeking more information on it. In spite of much research it is still doubtful whether serum hepatitis and infectious hepatitis are two diseases or one. They present very different epidemiological pictures, but little is yet known about the viruses associated with them.

Blood and all its derivatives, with the probable exception of gamma globulin, carry a risk of transmitting hepatitis in proportion to the number of blood donors who have contributed to the pool. Apart from keeping to a minimum the numbers of donors contributing, the risk can be slightly reduced by rejecting donors who have a history of jaundice. Fibrin foam and albumin may be made safe if adequately heated. It was hoped that ultra-violet irradiation of plasma might be an effectual preventive, but there is now evidence that it is not entirely so. The risk of transmitting hepatitis is attached not only to blood products but also to parenteral injections with inadequately sterilized syringes and needles. Adequate sterility is not easy to attain, for the virus

1 *Wld Hlth Org. techn. Rep. Ser.*, 1953, No. 62. Geneva.
2 *J. Amer. med. Ass.*, 1951, **147**, 714.

shows remarkable powers of resistance to most physical and chemical agents. Laboratory experts are apt to criticize the general practitioner for his undoubtedly imperfect methods of syringe sterilization, but the experts have yet to persuade everyday users that the recommended techniques are safe, economical, and practical in the surgery and the home.

Serum hepatitis appears to spread only by parenteral injections, whereas infectious hepatitis, like other infections transmitted by food and drink and by direct contact, is a problem of communal life. With dysentery it has been the scourge of armies and is now a plague of institutions and nurseries. The case fatality rate is low but by no means negligible. About 200 people in Great Britain die of it each year. It is a long and unpleasant illness and may be a prominent cause of chronic liver disease. General measures of hygiene may not help much to control it, but there is now good evidence that gamma globulin is a useful prophylactic. The most recent report comes from Stokes and his colleagues[2] in the U.S.A. Controlled trials were conducted in three communities—a mental colony, a hospital, and a children's home. Few cases of jaundice occurred among those protected by globulin, though a high proportion of untreated patients were attacked. The investigators made two further observations of great importance. They found that people were protected by 0.01 ml. of gamma globulin per pound of body weight (0.02 ml. per kg.), a much lower dose than is generally thought necessary. Moreover, the immunity appeared to last much longer than is usually expected with simple passive immunization. The authors explained this by suggesting that active immunity resulted from an inapparent infection under the cover of passive immunity. The far-reaching significance of this hypothesis, and its possible application to diseases other than infectious hepatitis, demand that further studies should be carried out to confirm their findings.

Gamma globulin is prepared in Great Britain by a different method from that used in the United States. The state of immunity of our blood donors to infectious hepatitis may also be different. We therefore cannot conclude from American trials that our gamma globulin would be equally efficacious. Institutional outbreaks of jaundice are not infrequent, and advantage should be taken of them to investigate this important question.

SIR HENRY WELLCOME

An exhibition commemorating the centenary of Sir Henry Wellcome's birth at Almond, Wisconsin, on August 21, 1853, was opened last week at the Wellcome Research Institution in London. It traces the history of Wellcome's early frontier days, when his family was nearly wiped out by Sioux Indians; of the time as a young man in America when he was a pharmaceutical student and a highly successful commercial traveller in pharmaceutical products; of the start of the firm of Burroughs, Wellcome and Co., established in London to exploit Silas Burroughs's "compressed medicinal powders"; and of the great scientific and practical enterprises which sprang from the success of Wellcome's business. In 1924 Wellcome consolidated his various pharmaceutical interests into a single company, the Wellcome Foundation. He died in 1936, four years after receiving a knighthood, and he directed in his will that the shares should be vested in five trustees who were to use the profits for the advancement of research in medicine. The Foundation maintains various laboratories where research work in physiology, chemistry, tropical medicine, and veterinary medicine is conducted. It also provides for the maintenance of a teaching museum of medical science, a historical medical museum, and a library which contains about 200,000 volumes and is one of the richest collections in the world of historical medical books. There is much of interest about Sir Henry Wellcome's colourful life in the short biographical memoir which has just been published by the Wellcome Foundation.

Dr. W. G. Wyckoff, scientific attaché to the American Embassy, spoke at the opening of the exhibition on behalf of the American Ambassador, who had been recalled to Washington. In the past, he said, basic research had been supported by a few wealthy and interested individuals. This was no longer sufficient, for such individuals were fewer and costs had greatly increased. But help from Governments, although needed in increasing amounts, was by far from being an ideal solution, and Sir Henry Wellcome's experiment had been a most successful one. Sir Henry Dale, chairman of the Wellcome Trust, described the activities which had been undertaken by the Trust. Research fellowships in pharmacology had been established in conjunction with the Pharmaceutical Society and in veterinary medicine with the Animal Health Trust. Two chairs had been endowed in the University of London: in tropical medicine at the London School of Hygiene and Tropical Medicine, and in pharmacology at the School of Pharmacy. The tropical medicine laboratory in Salonika was enlarged before the second world war; following the German invasion and the dislocation of the civil war the Trust had financed the small band of exiled staff from this laboratory who were doing fine work in Kenya. Grants had been made to medical laboratories in Australia and New Zealand. £100,000 had been given for the new Wellcome Pathological Museum at the Royal College of Surgeons and £125,000 for the Wellcome Research Library at the Royal Society of Medicine. Publication grants had been made to the Royal Society in aid of publication expenses in medicine and allied subjects. Capital had also been set aside for the publication of a complete catalogue of the Wellcome Historical Medical Library up to 1850. The Trust, Sir Henry Dale concluded, had not yet reached its full range of activity, but it had already spent half a million pounds in carrying out its founder's intentions. Sir Henry's speech left no doubt that the Foundation will continue to build up its already great reputation for research and munificence.

Sir Cecil Wakeley was re-elected President of the Royal College of Surgeons of England on July 9. He was first elected President of the College in 1949.

REFRESHER COURSE FOR GENERAL PRACTITIONERS

SCROTAL SWELLINGS

BY

R. J. McNEILL LOVE, M.S., F.R.C.S.

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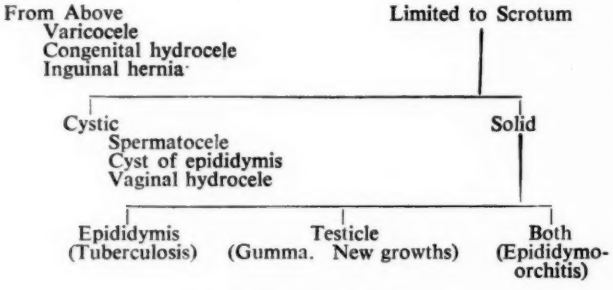
Scrotal swellings are commonly encountered in general practice, and a preconceived scheme for clinical examination is a practical help to accurate diagnosis. Thus the clinician must first decide whether the swelling is passing into the scrotum from above or whether it is entirely contained in the scrotum. If the latter, is the swelling cystic or solid, and, if solid, is it in the epididymis or the testicle or are both the epididymis and testicle involved? With these points in mind, the following simple scheme comprises a summary of scrotal swellings:



Swellings from Above

These are usually easy to recognize and can be dismissed in a few words. Thus an inguinal hernia may be reducible either by the patient or by the clinician, preferably with the patient recumbent. If the hernia is irreducible it can easily be palpated as it emerges from the external ring on its way to the scrotum.

A varicocele is usually of long standing and classically resembles a "bag of worms." Should the varicocele be of recent origin the possibility of compression of the spermatic veins by a renal tumour must be borne in mind.

A congenital hydrocele is one in which the processus vaginalis persists, so that peritoneal fluid can escape along the inguinal portion of the scrotal sac. Pressure on the scrotal part of the hydrocele causes a bulge along the inguinal canal, but fails to reduce the fluid owing to an "inverted ink-bottle" effect at the internal ring. However, the history is typical in that the scrotal swelling is smaller in the morning, as during recumbency some of the fluid seeps back into the peritoneal cavity along the processus vaginalis. Tapping such a hydrocele is useless, as more fluid will trickle down from the peritoneal cavity and so cause recurrence of the swelling; this it can be cured only by excision.

Cystic Swellings

Spermatocele.—This is a retention cyst in a vas efferens. The nature of the obstruction is open to conjecture, but it is congenital, or traumatic, or inflammatory. Typically, a young adult presents himself with a globular painless cystic swelling situated above the testicle. Patients may even flatter themselves that they have been blessed with an additional testicle: in fact, a mediaeval Pope once granted an applicant permission to marry two wives because he had three "testicles." A spermatocele varies in size from a pea to a plum and only exceptionally continues to enlarge after this dimension is reached. The patient should be advised to ignore the cyst; but, if it worries him, aspiration is easily performed. The fluid thus obtained contains dead and dying spermatozoa and resembles barley water in appearance.

Cyst of the Epididymis.—This condition is due to cystic degeneration occurring in the paradidymis, or organ of Giraldès. These vestigial remains are analogous to the tubules (organ of Rosenmüller) which sometimes persist in the broad ligament and give rise to a cyst in that structure. A cyst of the epididymis may closely resemble a spermatocele, but two points may help the clinician in distinguishing the two conditions. A "cyst" of the epididymis is actually a collection of cysts, and therefore, on careful palpation, more closely resembles a bunch of small grapes rather than a single grape. Moreover, congenital conditions are often bilateral; therefore cysts of the epididymis may present symmetrically, whereas it would be a remarkable coincidence if a vas efferens on both sides became obstructed.

The differential diagnosis of these two conditions has a practical application in their treatment. As already mentioned, a spermatocele is a single cyst and therefore may very properly be treated by aspiration (although cure is not guaranteed), but it is manifestly futile to attempt to empty a bunch of cysts by this method. If necessary a cyst of the epididymis is removed by careful dissection so as to preserve the spermatic vessels, and it will be noted that the contained fluid is crystal clear.

Hydrocele.—Acquired hydroceles are either primary, or secondary to some underlying conditions. A *primary, or idiopathic, hydrocele* is probably the commonest scrotal swelling. It is easily diagnosed in that the cystic swelling surrounds the testicle, and, unless the wall is thickened or, very exceptionally, calcified, transillumination is obvious, Repeated tapping causes some oozing into the sac, and organization of blood clot may increase the thickness of the sac so that it eventually diminishes in translucency. As mentioned below, if the hydrocele is large enough to prevent adequate examination of the testicle it should be tapped so that any underlying pathological condition can be recognized. Repeated tapping may keep a hydrocele under control, but excision of the sac is a simple procedure which guarantees a cure. *Secondary hydroceles* are due to some pathological condition of the testis or epididymis. In most cases only a small quantity of fluid is present, so that the diagnosis is not unduly obscured. However, there is one condition in which a secondary hydrocele may be of such size that the underlying testicle cannot be palpated and the unwary clinician may diagnose a primary hydrocele and assume that the testicle is normal. Thus the increasingly rare gumma may present itself under these conditions, and it should be the rule that when a middle-aged patient presents himself with a hydrocele large enough to obscure the testicle the fluid should be withdrawn and the condition of the testicle assessed by an experienced surgeon.

Solid Swellings

Epididymis.—Tuberculous infection is a not uncommon cause of epididymal enlargements. If the disease progresses the testicle itself may eventually be destroyed, but it rarely increases in size. In the early stages the epididymis is firm in consistency and irregular in contour—commonly known as "craggy." The condition is comparatively painless, so that the patient may ignore it until an abscess erodes the skin and the discharge therefrom impels him to seek medical

advice. Further clinical examination may reveal a "beaded" vas due to submucous tubercles in the duct, and on rectal examination tuberculous nodules are commonly palpated in the prostate or seminal vesicles. Needless to say, a comprehensive examination of the patient is essential in order that appropriate treatment may be applied to other regions, notably the kidneys and lungs, which may be similarly affected. In the early stages many cases respond well to streptomycin, but if sinuses occur epididymectomy or orchidectomy will be required.

Testicle.—Enlargement of the body of the testis is due to either a gumma or neoplasm. *Gummata* are now rare, and for that reason are all the more apt to be forgotten. As already mentioned, a gumma may be concealed by a hydrocele. It presents itself as a smooth and entirely painless swelling. The absence of pain is due to replacement of normal cells by fibrous tissue. If the gumma breaks down it becomes adherent to the anterior surface of the scrotum and may eventually erode through the skin. If a gumma is suspected a clinical examination of the patient will probably reveal other evidence of tertiary syphilis, notably one of the stages of chronic superficial glossitis (especially leucoplakia), perforation of the hard palate, scarring of the soft palate, or evidence of previous subcutaneous gumma in the form of silvery, supple, and serpiginous scars, classically likened to "tissue paper," and which are commonly found on the thighs and upper part of the legs. Recent gummata readily respond to antisyphilitic treatment, but if the testicle has been destroyed and replaced by fibrous tissue then excision is advisable.

Teratoma of the testicle. The patient succumbed with pulmonary metastases. (From R. J. McNeill Love's *Minor Surgery*, by permission of H. K. Lewis and Co.)

Excluding curiosities, the two malignant diseases affecting the testis are seminoma and teratoma. A *seminoma* is a rapidly growing carcinoma of the seminiferous tubules. It sooner or later becomes irregular in shape and consistency, owing to local areas of degeneration and haemorrhage. Dissemination is mainly by lymphatics, and para-aortic lymph nodes in the epigastrium are commonly involved, as it is at this level that the testicle develops before it slides down into the scrotum. Fortunately a seminoma is radiosensitive, and modern treatment consists in a high castration and deep *x*-ray therapy to the regional lymph nodes. A *teratoma* may be present for years as a firm, globular swelling (formerly known as fibrocystic disease), but in due course malignant changes supervene as shown by recent increase in size (see Fig.). Its consistency is usually firmer than that of a seminoma, and the history of a previous long-standing swelling also helps to distinguish the two conditions. This is of prognostic importance, as the malignant teratoma disseminates by the blood stream, notably to the lungs. Also, it is comparatively radio-resistant, so, if dissemination has occurred, the prognosis is hopeless. Teratomata at any stage must be removed immediately, in the hope that dissemination has been forestalled.

Testicle and Epididymis.—Acute gonococcal epididymo-orchitis would be but a memory if patients sought early treatment. Acute, subacute, or chronic epididymo-orchitis may occur in connexion with infections of the urinary tract, especially a low-grade cystitis associated with prostatic obstruction. Occasionally, epididymo-orchitis occurs for no discoverable reason, and this is attributed either to a haematogenous infection or to regurgitation of urine along the vas deferens. This condition is said to occur when the patient has made some strenuous physical effort while the bladder was distended. In severe cases the patient should be confined to bed for a few days with support to the scrotum and kaolin poultices applied.

Finally, there is one condition which may closely resemble some of these already mentioned, the physical characters of which vary according to the stage at which the patient is seen. A *haematocele* is commonly due to a blow which the patient is unlikely to forget, and, although the swelling somewhat resembles a hydrocele, the history of injury and lack of transillumination settle the diagnosis. Evacuation of the blood through a small incision at the neck of the scrotum is prudent, otherwise the subsequent clot will require months to absorb and haematogenous infection may be a tiresome complication. Curiously enough, a haematocele can occur quite insidiously and in this case errors of diagnosis are likely, as the patient may not seek medical advice until the testis is surrounded by clotted blood. There is no history of injury and the physical signs closely resemble those of a seminoma. To emphasize this point, my former chief, Russell Howard, who was surgeon to the London Hospital, never tired of telling students that he had, after careful consideration, wrongly diagnosed three successive cases. As with any condition in which malignant disease cannot be excluded, exploration is essential. If a recent haematocele is discovered the blood is evacuated. In later stages organization of clot will compress the spermatic vessels and cause testicular atrophy, so excision of the tunica vaginalis, including the clot and testicle, removes a useless encumbrance.

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ORDER OF ST. JOHN OF JERUSALEM

The *London Gazette* has announced the following promotions in, and appointments to, the Venerable Order of the Hospital of St. John of Jerusalem:

As Knight: Dr. G. P. Huws. *As Commanders (Brothers):* Surgeon Rear-Admiral T. N. D'Arcy, C.B., C.B.E., L.R.C.P.& S.Ed., Surgeon Commander D. P. Gurd, R.N., Air Vice-Marshal V. S. Ewing, C.B.E., M.B., Mr. W. M. Brennen, F.R.C.S., Drs. R. Davies-Jones, T. W. David, and H. J. Porter. *As Officers (Brothers):* Surgeon Captain E. H. Lee, M.D., Brigadier K. A. Hunter, O.B.E., C.D., M.D., Colonels J. Huston, M.B., F.R.C.S., R. A. Bennett, M.D., F.R.C.P., R. T. Shipman, M.R.C.S., L.R.C.P., R.A.M.C., Lieutenant-Colonels B. C. Hardiman, E.D., M.D., and E. J. Selby, O.B.E., M.R.C.S., L.R.C.P., Group Captain J. F. Dales, M.R.C.S., L.R.C.P., Messrs. W. E. Gallie, M.D., LL.D., F.R.C.S., and A. R. F. Hubbard, F.R.C.S., Drs. C. W. Walker, I. H. Lloyd, C. O. S. B. Brooke, W. K. Hay, G. F. Sleight, O.B.E., W. R. Cambridge, W. H. Cruickshank, J. A. Cochrane, J. T. Daly, E. A. Renner, O.B.E., and J. P. McGuigan. *As Officer (Sister):* Dr. Florence E. Sexton. *As Serving Brothers:* Surgeon Captain T. B. McLean, C.D., M.D., Surgeon Commander T. W. Froggatt, M.B., Colonel J. N. B. Crawford, M.B.E., M.D., Group Captain B. R. Brown, M.D., Mr. D. O. Clark, M.B.E., M.B., F.R.C.S., Drs. W. T. Currie, G. M. Lloyd, D. F. Torrens, W. H. Gray, S. F. Fouracre, J. J. Brennan, S. N. Chopra, G. H. Collier, J. E. Thomas, S. W. McCarthy, F. L. Ralphs, I. A. Balmer, W. W. Bell, J. E. Hiltz, J. H. W. Hutchinson, and L. W. Pritchett. *As Serving Sisters:* Drs. Eluned Evans and Hilda M. Shand.

BRITISH EMPIRE CANCER CAMPAIGN

Lord Horder, chairman of the Grand Council, presided at the annual general meeting of the British Empire Cancer Campaign which was held in London on July 7. After reading a message from the Duke of Gloucester, president of the Campaign, Lord Horder reported the results of a questionary sent to general practitioners on whether they were in favour of cancer education for the public. He said that 24% of those approached had replied, 2,149 being in favour of it and 2,683 against (see also Lord Horder's letter on p. 148). It would clearly be premature, therefore, for the Campaign to take any action in this matter at present.

Substitution Therapy for Cancer Control

Proposing the adoption of the annual report,* Professor Alexander Haddow, director of the Chester Beatty Research Institute at the Royal Cancer Hospital, said that the field of interest in cancer research had now been greatly widened to include not only the carcinogenic agents themselves but also the giant molecules within the cell with which it was believed that they combined. It appeared that the cancer cell was derived from the normal cell through the loss of enzyme or ferment systems normally responsible for growth regulation. He hazarded the prediction that sooner or later there would come something entirely new in the chemotherapy of cancer—a kind of substitution therapy by which the cancer cell would be controlled from without, by the same kind of chemical means as the normal cell automatically regulated itself from within. The prospects had sensibly changed: even cancer prevention, which only a few years ago seemed utterly beyond our hopes, might yet, with the development of all these trends, prove to be within our ultimate powers. One encouraging feature of the present approach to cancer was that it was of a more physiological kind than formerly; however, no explanation could be complete which failed to take account of all the facts, including the existence of undoubted tumour viruses. "It may well be that the history of cancer research will resolve itself into two main phases: first, the impartial exploration of every avenue of attack; secondly, the definition and limitation of those few approaches which are decisive in strategy," said Professor Haddow. "It seems to me we may shortly be moving from the first of these phases to the second."

The Campaign's Nuffield Trophy was awarded to Wells in Somerset, which last year raised £720 19s., approximately 2s. 6d. per head of the population, for the Campaign. The meeting ended with a vote of thanks to Lord Horder, proposed by Lord Webb-Johnson.

KING EDWARD'S HOSPITAL FUND FOR LONDON

The Duke of Gloucester presided at the 56th annual meeting of King Edward's Hospital Fund for London, held last week at the House of Lords. He reviewed the Fund's activities during the five years since the inception of the National Health Service.

During this time a good part of the energy and money of the Fund had gone into building up a series of educational ventures. With the inauguration in the autumn of the first course for prospective matrons the present series would be complete. They did not propose now to introduce any fresh training schemes in the next few years but rather to consolidate those to which they were already committed. If the different members of hospital staffs could be encouraged to work closely together something really important would have been achieved.

For a time after the start of the Health Service it had seemed that grants to hospitals would be mainly for amenities, in a somewhat narrow sense of that word. Now things were changing, and the demands on the distribution committee for grants were certain to grow. Grants were being given for the provision of hospital gardens and for recreation huts for hospital staffs. The Fund was reverting to the earlier system of the visiting of hospitals by doctors and laymen working in pairs. These visits had been warmly welcomed by the hospitals.

The provision of homes for aged sick patients from hospitals had made further progress, and the homes continued to attract notice as a pioneer effort to help the hospitals. They had recently opened one such home specially intended for nurses who had themselves become patients in the hospitals, often for long periods. The home was on the edge of Hayes Common in Kent and would be run by the London Hospital. Another way of relieving the pressure for hospital accommodation for old people was to make full use of the services of the various voluntary agencies. The Fund had encouraged this, and for the last two years had been giving a special grant to the South-east Regional Hospital Board to allow the close personal liaison with these agencies that was so essential in getting results. The Fund was now considering how this help might be extended to the other Regions. In conclusion, the Duke of Gloucester referred to the way in which the Emergency Bed Service had handled the crisis last winter. The warning system had certainly worked well and was now likely to become a permanent feature of the arrangements.

Sir Edward Peacock, the treasurer, said that the total income for 1952 had been £467,000. Grants to hospitals and convalescent homes totalled £171,000, a further £100,000 had been set aside for Homes for the Aged Sick, and £95,000 had been absorbed by the various staff colleges and other activities administered by the Fund itself.

To conclude the business, Sir Ernest Pooley, chairman of the management committee, presented the draft annual report; and Sir Frederick Messer moved a vote of thanks to the Duke of Gloucester.

CLINICAL RESEARCH AND THE HEALTH SERVICE

The following is a summary of the recommendations in the recently published White Paper on "Clinical Research in Relation to the National Health Service" (see also p. 140). This report was prepared by a joint subcommittee of the Medical Research Council and the Standing Medical Advisory Committee of the Ministry of Health, and it has the approval of the Advisory Committee on Medical Research in Scotland.

Recommendations

1. A central organization for the promotion of clinical research is necessary and should be established as part of the Medical Research Council. A Clinical Research Board should be appointed by the Medical Research Council, after consultation, and in agreement, with the Health Departments. The Medical Research Council should be the financial authority for centrally organized clinical research and would be the employing authority of the research workers engaged on its projects.

(*a*) The central organization for clinical research should work in close liaison with the Health Departments and the clinical departments of the universities.

(*b*) Additional funds should be made available to the board at an approximate figure of £50,000 for the first year, rising to £250,000 in three or four years' time.

(*c*) The central organization should be set up before any new arrangements are made for decentralized research financed from Exchequer funds.

(*d*) The above scheme should be reviewed after a trial period of three years.

2. Provision should be made for decentralized research at the level of regional hospital boards and boards of governors and hospital management committees. As this

*British Medical Journal, 1953, 2, 93.

research would arise mainly from, and would be closely related to, medical practice, it should be financed either by the Ministry of Health from National Health Service Funds or by local bodies from their own resources.

(*a*) Within this field there should be the greatest possible freedom from detailed supervision.

(*b*) Responsibility for the distribution of Exchequer moneys for research purposes should lie with regional hospital boards and boards of governors. Each board should set up a research committee after consultation, and in agreement, with the associated university or medical school, to advise on the spending of the research budget.

(*c*) In determining the amount of Exchequer money to be allocated to boards, regard should be had to the amount of endowment moneys available locally.

(*d*) Annual progress reports should be submitted to the Ministry of Health, who would seek the advice of the central organization for clinical research upon them.

(*e*) Advice from this central research organization might be sought on schemes financed from endowment funds.

3. Careers in clinical research should be equated with careers in the National Health Service. They should confer the same status, carry the same salary and superannuation rights, and entitle the holder to the same distinction awards.

(*a*) There should be opportunity for free interchange of staff without loss of status, remuneration, or prospects. In particular, provided it were insisted that appropriate clinical training and responsibility were being continued, junior posts in clinical research should rate for seniority in the same way as National Health Service posts in the corresponding branch of medicine.

(*b*) (i) Whole-time research workers within the central research organization above the grade of Senior House Officer should be employed and paid by the Medical Research Council on the recommendation of the Clinical Research Board. (ii) Regional boards and boards of governors should appoint, on the recommendation of their research committees, only research workers up to and including the grade of Senior Registrar.

(*c*) Clinical research units should be set up and administered as part of the central research organization and situated at particular hospitals on the basis of mutual arrangement.

(*d*) Clinical research workers employed by the Medical Research Council should be regarded as members of the Council's staff placed at particular hospitals by mutual arrangement.

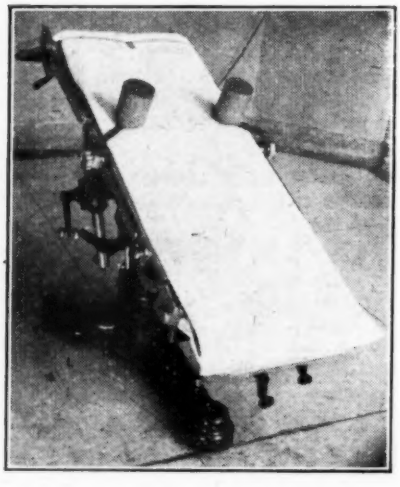
(*e*) Any criteria for determining the training of consultants and specialists should recognize research and clinical experience in a field of clinical research as appropriate training for according full consultant or specialist status in that particular field.

4. Provision should be made for appropriate workers to carry out clinical research abroad.

Preparations and Appliances

PELVIC RESTS

Dr. F. G. WOOD-SMITH, Department of Anaesthetics, Postgraduate Medical School of London, writes: The grave danger of producing brachial plexus palsy by suspending a patient by means of shoulder-rests in operations in the Trendelenburg position has given rise to a search for other means of suspension. Ogier Ward has designed pelvic rests which are in many ways satisfactory. They are, however, somewhat difficult to adjust; the rubber supports which grip the patient are apt to interfere with the surgeon when the incision is laterally placed, and the supports may swivel, with the result that the patient slips down the table.



The pelvic rests here described are simple and easy to fix, and have given satisfactory service at the Hammersmith Hospital for some months. They have been used with the Lloyd-Davies supports for synchronous combined abdominoperineal resection of the rectum and most other operations in the Trendelenburg position. They consist of a pair of angle brackets (see Fig.) that fit into the standard slides which normally carry the operating-table lithotomy arms. The reverse end of the bracket is fitted with a sponge-rubber-covered block which fits into the patient's loin above the iliac crest. By adjusting the locking nut on the slide the angle and height of the bracket can be altered to fit individual patients. The height of the block should be flush with the anterior superior spine of the pelvis, and the angle of the bracket 45 degrees approximately with the long axis of the table (see Fig.).

I am indebted to Mr. M. Ewing for his advice and criticism in the testing of these rests, and to Messrs. Allen and Hanburys for the production of the prototypes. The rests are now in production and may be obtained from the above firm.

Correspondence

Because of the present high cost of producing the Journal, and the great pressure on our space, correspondents are asked to keep their letters short.

Cancer and the Public

SIR,—The British Empire Cancer Campaign has on several occasions considered the question of lay education in cancer as a means of earlier diagnosis of the disease. It will be realized that this question is a difficult one and one which meets with opposing views among both medical men and laymen. Those who favour a campaign of intensive lay education in cancer argue that even at the worst it must bring to light some cases in the earlier and potentially curable stage, and that in any case a policy of diffusing knowledge is more likely to abolish, than to create, fear, which they feel is largely born of ignorance.

Those who take the opposite view argue that the early diagnosis of cancer is unlikely to be appreciably affected by a campaign of lay education; that the best course at the present time is the strengthening of the relation between patient and family doctor; and that a policy which risked the danger of producing cancer neurosis in the population might render the family doctor's task more difficult. This might happen in two ways: first, by fear engendered by the propaganda keeping some genuine cancer cases away, and, secondly, by overloading the doctor with cases of cancer phobia.

As a step in its inquiries, the British Empire Cancer Campaign recently decided to take the opinion of the general practitioners of the country. All general practitioners in Great Britain and Northern Ireland were circulated and asked to give an answer to the following question: "Do you consider that the launching of a scheme of lay educational propaganda on cancer (by pamphlet, lectures, films, etc.) would be of assistance in securing the earlier diagnosis of cancer, and thereby improving the chances of a cure? Please answer 'Yes' or 'No.'"

21,040 letters were sent out and there were 5,053 replies, a proportion of 24%, which is a particularly high proportion of replies to a circular letter. Of the replies, 2,148 were an unqualified "yes" and 2,683 an unqualified "no." In the qualified answers, the main qualification was that the scheme would only be possible with increased facilities.

Others were of the opinion that the scheme should be limited in scope and conducted with great care to avoid a phobia. Accompanying letters showed that a large number of practitioners had given much thought to the matter.

The British Empire Cancer Campaign will consider the matter further in the light of this expression of general-practitioner opinion. In the meanwhile, the campaign expresses its gratitude to general practitioners in the country for replying in such large numbers. This is an index of the interest which the problem arouses.—I am, etc.,

London, S.W.1. HORDER,
Chairman, British Empire Cancer Campaign.

Antibiotics and Hospital Staffs

SIR,—Referring to the recent communication of the Ministry of Health (*Journal*, July 4, p. 39) concerning the incidence of sensitivity in nursing staffs handling antibiotics, I would like to draw attention to another side-effect found in hospital dispensers preparing penicillin solutions.

Some time ago the dispenser of the Royal Infirmary, Edinburgh, drew my attention to the fact that three girls dealing with the preparation of penicillin solutions had developed black tongue. It had naturally caused some anxiety to the persons concerned. As care was always taken to use long tubing between the pipette and the operator's mouth the discoloration was due most probably to inhalation rather than actual deposition of penicillin solution in the mouth. The examination of lingual scrapings revealed in all three cases a very scanty bacterial flora but no fungi. Advice was given to interpose a filter consisting of a length of glass tubing packed with cotton wool in the rubber tubing connecting the pipette and the mouthpiece. This device was successful in causing disappearance of the brown discoloration, which has not recurred.—I am, etc.,

Edinburgh. W. TOMASZEWSKI.

SIR,—The articles and news that have appeared in the *Journal* of July 4 (pp. 30 and 39) prompt me to describe the desensitization of a nurse who became sensitive to streptomycin after giving it for several years.

This nurse, a girl of 22, reported to me in December, 1952, complaining of swollen eyelids, conjunctivitis, and puffy lips, with a raised erythematous rash over the upper part of her chest and forearms. These manifestations occurred if she as much as made six beds which had contained patients receiving streptomycin. She was able, however, to work in the linen-room without trouble. A misguided test injection of 50 mg. of streptomycin sulphate produced symptoms as above, but of alarming severity, which were not improved by the exhibition of several antihistamines in large doses.

After much discussion it was decided to attempt desensitization, though not much hope was held out for success. Accordingly we began with a dose of 50 micrograms, proposing to double the dose every other day. In the event it was found necessary to repeat a few doses at the same strength, as a slight reaction occurred. The streptomycin—in the sulphate form—was made up in the dispensary freshly each week, and of such dilutions that the injections never exceeded 0.2 ml. until the larger doses were reached. At first the injections were made subcutaneously, but later were given intramuscularly. The largest dose given was 0.8 g. of streptomycin—it being considered unnecessary to go beyond this.

After the course of desensitization the nurse was returned to full ward duties, which include the giving of streptomycin in both the sulphate and dihydro forms. She very occassionally complains of puffy, cracked lips, but this seems to be associated with the use of lipstick. She has no other allergic tendencies that I can discover, but her father is said to have suffered from asthma.—I am, etc.,

Newdigate, Surrey. W. F. WHEELER.

Tropical Diseases in Britain

SIR,—The omission of onchocerciasis from your annotation (May 16, p. 1096) is unfortunate, if only because irreparable damage may occur before the disease is suspected.

I would warn my ophthalmic colleagues in Britain to bear this condition in mind, the more so because in the initial stages the symptoms may be trivial. A recent case of "glare asthenopia" with 6/4 vision revealed a typical, though mild, nummular keratitis and numerous microfilariae in the aqueous of each eye.—I am, etc.,

Kampala, Uganda. A. J. BOASE.

SIR,—Professor W. Melville Arnott's views on the diagnostic use of emetine in amoebiasis (*Journal*, May 30, p. 1219) will be shared by many country practitioners in endemic areas and particularly in the non-operative diagnosis of deep-seated liver abscess. In this part of Africa, where primary hepatic carcinoma is not uncommon, liver abscess may occasionally give rise to confusion. In both the age incidence is the same—20–40 years as a rule—and a hard, lumpy epigastric swelling may closely simulate hepatic carcinoma, when in reality one is dealing with a small abscess surrounded by firm inflamed liver tissues. In the type of case of which one is thinking aspiration yields an ounce or so of thick greenish pus very unlike the classical anchovy sauce of larger and thinner-walled abscesses, and one remains in doubt as to the true diagnosis.

Liver biopsy would be helpful, but is not free from the risk of haemorrhage, not to mention the delay in obtaining a reliable report, but emetine will readily clarify the diagnosis and set both the liver and the doctor's mind at rest.—I am, etc.,

Nqutu, Zululand. ANTHONY BARKER.

Proguanil-resistant Malaria

SIR,—Dr. S. Avery Jones, in his article entitled "Experiment to Determine if a Proguanil-resistant Strain of *P. falciparum* Would Respond to Large Doses of Pyrimethamine" (*Journal*, May 2, p. 977), expresses the hope that special care will be taken that men of the King's African Rifles serving in Malaya do not return to East Africa with gametocytes of Malayan strains of malaria in their blood. I hasten to assure him that such steps are taken. Amongst African troops the incidence of malaria is extremely low. Sir Neil Hamilton Fairley on a recent visit to Malaya referred to this fact as "a remarkable achievement."

African troops, who are on suppressive mepacrine, continue to take a tablet of the drug (0.1 g.) daily for four weeks after leaving Malaya. Any of them who have developed benign or quartan malaria in Malaya receive a standard course of quinine and pamaquin or of chloroquine and primaquine if this has not already been carried out. At the conclusion of this course of treatment suppressive mepacrine is continued for four weeks after leaving Malaya.—I am, etc.,

Singapore. E. J. CURRAN,
Deputy Director of Army Health, G.H.Q., Far East Land Forces.

Polyarthritis in Rubella

SIR,—I was interested in the account by Dr. I. S. L. Loudon (*Journal*, June 20, p. 1388) of the occurrence of polyarthritis in association with German measles in adults.

I had a similar experience during an epidemic of German measles in March of this year, which involved 30 children and 7 adults. In all the children and two male adults the infection was of the usual mild type. In all five female adults, whose ages ranged from 30–45, and who were all infected by their own children, the infection was severe with marked conjunctivitis and photophobia, a florid rash, a painful generalized adenitis, muscle pains, and polyarthritis. In one case the polyarthritis was so severe that she was afraid to turn over in bed. In all cases the arthritis cleared completely after a duration of 5–10 days.

In my experience muscle pains are an almost invariable accompaniment of German measles in the adult, but I have not previously seen an associated polyarthritis.—I am, etc.,

Leeds. G. W. LEWIS.

Non-fatal Meningitis Due to Friedländer's Bacillus

SIR,—In the *Journal* of May 30 (p. 1204) Dr. W. J. D. Eberlie published particulars of a case of meningitis due to Friedländer's bacillus with recovery. Meningitis due to this organism is rare and recovery rarer still. It may be of historical interest if I give you a few details of a case of non-fatal meningitis due to Friedländer's bacillus, the particulars of which were published in the *Proceedings of the Transvaal Mine Medical Officers' Association* in July, 1936.

The patient was a young African mine labourer aged about 19 years. He showed the typical signs of meningitis when he was admitted to hospital on March 24, 1936, with a temperature of 104.8° F. (40.45° C.). At lumbar puncture 45 ml. of turbid fluid was withdrawn; 25 ml. of anti-meningococcal serum was injected intrathecally. At a second lumbar puncture the following day, 50 ml. of turbid fluid was withdrawn and 25 ml. serum given, this being the recognized treatment in those days before the advent of antibiotics. Three days after admission to hospital he developed an acute exudative iritis of the left eye. On the fifth day of his stay in hospital he developed an acute synovitis of the left knee-joint. The joint was aspirated once and 52 ml. of turbid fluid was withdrawn. Laboratory investigation revealed the presence of Friedländer's bacillus in the cerebrospinal fluid, in the fluid from the knee-joint, and in a smear taken from the conjunctival sac of the left eye. The patient made a complete recovery and was discharged from hospital three weeks after admission. There were no sequelae.

Dr. J. H. S. Gear, Deputy Director of the South African Institute for Medical Research, did the bacteriological examinations in this case, and he was satisfied that the organism was Friedländer's bacillus. At the time he submitted a very complete and detailed report of his investigations.

The points of interest in this case are: (1) It occurred before the days of antibiotics, and recovery took place in spite of not having the very great advantage of treatment with these modern remedies; (2) the patient was never critically ill as would be expected in a Friedländer's bacillus infection; (3) the complications: (*a*) acute exudative iritis of the left eye from which he recovered completely; Friedländer's bacillus was found in a smear from the eye; (*b*) acute synovitis of the left knee-joint. The joint condition subsided with one aspiration, and there was no permanent disability. Friedländer's bacillus was isolated from the joint fluid.—I am, etc.,

Roodepoort, Transvaal. L. E. MILLER.

Effect of Dried Liver on Growing Children

SIR,—I reported last year[1] that when apparently normal nursery-school children were given a special preparation of dried liver over a period of three months they showed an appreciable and significant improvement in growth as indicated by their gain in height and weight. There is reason to believe that this was brought about by a dietary factor (not vitamin B_{12}) apparently deficient in the diets of the children, rather than by some "unnatural" stimulation of growth.[2]

Since the original report appeared, I have often been asked about the subsequent rate of growth of these children. As indicated at the time, many of the children have been leaving the nursery schools, so that it was probable that relatively few of the original 60 could be seen again. Nevertheless, it seemed worth while to measure again as many as were still available. This has now been done.

The children were examined in June, 1953, just two years after the experiment had begun. It was possible to find 12 children ("L" group) who had received the supplement (five boys, seven girls) and eight children ("C" group) who had acted as controls (two boys, six girls). In the 21 months from the end of the experiment, the mean increments in height and weight were 12.1 cm. and 1.45 kg. for the "L" group, and 12.5 cm. and 1.50 kg. for the "C" group. These are equivalent to 4.75 in. and 3 lb. 3 oz. for the "L" group, and 4.9 in. and 3 lb. 5 oz. for the "C" group. There is no significant difference between the two groups.

Within the limits set by the small number of children who have been re-examined, therefore, we can state that the rate of growth during the last 21 months has been the same for the two groups. The increased growth of the children who received the supplement over the controls which was produced by the liver two years ago has been kept; since that time there has been neither continued more rapid growth nor a compensatory decline in the rate of growth.—I am, etc.,

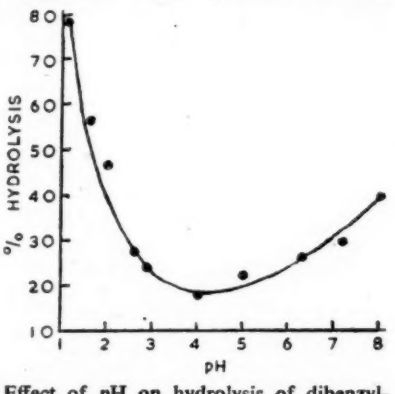
London, W.8. JOHN YUDKIN.

REFERENCES

[1] *British Medical Journal*, 1952, **1**, 1388.
[2] Yudkin, J., *Postgrad. med. J.*, 1953, **29**, 112.

Oral Penicillin

SIR,—In your leading article, "Oral Penicillin" (*Journal*, April 11, p. 823), you comment that it is puzzling that a penicillin compound (N,N'-dibenzylethylenediamine dipenicillin G) of such low solubility, with consequently a slow rate of absorption when injected, should be absorbed quite rapidly and regularly when swallowed. This question has also exercised us. A study, therefore, was made on the effect of *p*H on the hydrolytic cleavage of dibenzylethylenediamine dipenicillin G. The results of this study, we believe, supply an adequate explanation for the "penicillaemia" after oral administration of the salt.



Effect of *p*H on hydrolysis of dibenzylethylenediamine dipenicillin G; 100 mg. suspended in 20 ml. Sorensen's buffer solutions. Temperature 37.5° C. for one hour.

From the chart it will be noted that the penicillin salt undergoes rapid hydrolysis at the *p*H of normal gastric juice and rather significant hydrolysis at slightly alkaline reactions. The soluble penicillin thus released would be available readily for absorption. The relatively slow rate of hydrolysis between *p*H 2.5 and *p*H 6.0 could account for a longer-continued absorption from the gastro-intestinal tract, and hence a more uniform if lower blood level for a longer time than would be obtained from a similar dose of soluble penicillin.—We are, etc.,

E. LOZINSKI.
C. H. GLEASON.

Montreal, Canada. The Research Laboratories, Charles E. Frosst & Co.

Who was Geminus?

SIR,—Dr. E. Ashworth Underwood in his admirable study "Medicine and the Crown" (*Journal*, May 30, p. 1185), and Professor G. A. G. Mitchell in his interesting letter (*Journal*, June 27, p. 1449), ask the question: "Who was Geminus?"

The answer is provided by the recent discovery by Professor E. G. R. Taylor of the will of "Thomas Lambrit als Geniny of the pricincte of the late blacke friers nighe Ludgate of London, booke printer . . ." In this document, which was registered and proved in the Prerogative Court of Canterbury (Index Library—*Wills of the Prerogative Court of Canterbury*, Vol. 111), there is only mention of his occupation as a book printer. He bequeathed to his brother, Jasper Lambrit, his property ". . . as lyeing and beinge within Leighe nighe unto Marke Wessett within the bishopryke of Leuke in the partes beyonde the Sea . . ." The location of this inheritance is not clear, but M. Henri Michel, of Brussels, interprets "Leighe" near "Marke Wessett" as "Lixhe," a village near the "border town of

Visé" within the bishopric of Liége ("Leuke" is Flemish). Mr. R. A. Skelton, Superintendent of Maps in the British Museum, drew attention to Professor Taylor's discovery in Lynam's *The Mapmaker's Art*, 1953. I am indebted to him for access to a photostat copy of this will, which can be seen in the Map Room.

Investigation of the clues furnished by this document will provide further biographical details of Thomas Lambrit (or Lambert), called Geminus, a master of many arts, and perhaps will arouse further "dilettantish interest."

As one of twins, I append my signature accordingly.—I am, etc.,

London, W.1. VALENTINE SWAIN (Geminus).

Orthopaedics and its Name

SIR,—I was interested in Dr. R. D. Lawrence's letter (*Journal*, June 13, p. 1335) headed "Orthopaedics and Its Name." I would, as author of the book *Chiropodial Orthopaedics* mentioned in the letter, like to raise two points. The first is that this book, amongst other things, is very much concerned with the correction of deformities in children's feet, and one chapter deals with the footwear of the child, and many of the clinical illustrations are of children and children's appliances. The other, as Dr. Lawrence will see if he refers to the preface, is that its title, although by no means perfect, is the best that could be devised in view of the present use of the words "chiropody" and "orthopaedics" and is not considered by myself to be in its final form.

If Dr. Lawrence or any of your correspondents can think of a better or more suitable title, their suggestions will be most welcome.—I am, etc.,

Manchester. FRANKLIN CHARLESWORTH.

SIR,—While I would not for a moment support Dr. R. D. Lawrence in his attempt (*Journal*, June 13, p. 1335) to complicate life by altering a name in established use, yet I must agree with him that the name should mean "the straight child."

Nicholas Andry, who coined the term, says in his *L'Orthopédie, ou L'Art de Prevenir et de Corriger dans les Enfants, les Difformités du Corps* (1741, Paris): "Quant au titre en question, je l'ai formé de deux mots grecs, scavoir, *d'Orthos* qui veut dire *droit*, . . . et de *Paidion*, qui signifie *Enfant*. J'ai composé de ces deux mots, celui *d'Orthopédie*, pour exprimer en un seul terme, le dessein que je me propose."—I am, etc.,

Birmingham. W. BRIAN GOUGH.

Prosthetic Mucosal Hypertrophy

SIR,—I was interested in Dr. J. Walter's article entitled "Prosthetic Mucosal Hypertrophy in the Mouth, Simulating Malignancy" (*Journal*, June 27, p. 1429).

Dr. Walter states that the only recent account he could find was one by Simmons.[1] I must point out, however, that I described this condition as "denture granuloma" in the *Practitioner* in 1939.[2] Subsequently, a description was published in both first and second editions of my textbook *Essentials of Surgery for Dental Students*.[3]

My purpose in raising this is that the term "denture granuloma" appears to be a simpler and more accurate designation than any other suggested.—I am, etc.,

J. COSBIE ROSS.

Liverpool.

REFERENCES

1 *British Medical Journal*, 1941, **1**, 119.
2 *Practitioner*, 1939, **143**, 113.
3 *Essentials of Surgery for Dental Students*, 1945 and 1952. Edinburgh.

Anticoagulants in Myocardial Infarction

SIR,—Dr. David Wheatley (*Journal*, June 20, p. 1391) supports my plea (*Journal*, May 30, p. 1233) for more energetic stimulation of the shocked patient after coronary infarction. At the end of his letter he disputes my contention that a reduction of prothrombin level to 60–75% of normal is adequate domiciliary treatment for coronary infarction.

I agree with Dr. Wheatley that *theoretically* the lowest reasonably possible prothrombin level is probably the best, but at the same time would call his attention to the following published series of cases. Wright *et al.*[1] treated 432 cases of coronary infarction with dicoumarol, and after the first three days, during which the dicoumarol had not full effect, found 6.5% of thrombo-embolic complications. Burt *et al.*[2] and Peters[3] conducted similar experiments, and each found a rate of about 6% of thrombo-embolic complications. Now the interesting fact is that Wright aimed at a prothrombin level of 10–20%, Burt of 20–30%, and Peters of 35–50%.

In my own smaller series of 60 cases in general practice[4] I found a rate of 5% of complications and aimed at a prothrombin level of 60–75%. So, although in some cases a level of 10–20% is advisable, I doubt if this is necessary in the majority. Support is given to this suggestion by the fact that after coronary infarction I kept 25 patients on dicoumarol at a prothrombin level of 60–75% of normal for periods of from six months to three years with one thrombo-embolic complication (4%). In the first year after infarction the pathologists Hellerstein and Martin[5] give a figure of about 45% for complications, and the clinicians Wright[1] and Barker *et al.*[6] give 36% and 44% respectively.—I am, etc.,

R. A. MURRAY SCOTT.

Leeds.

REFERENCES

1 *Amer. Heart J.*, 1948, **36**, 801.
2 *British Medical Journal*, 1949, **2**, 1250.
3 *J. Amer. med. Ass.*, 1946, **130**, 398.
4 *Lancet*, 1952, **1**, 488.
5 *Amer. Heart J.*, 1947, **33**, 443.
6 *Surgery*, 1945, **17**, 207.

Simple Depressed Fracture of the Skull

SIR,—I read with considerable interest the article by Professor Lambert Rogers on simple depressed fracture of the skull (*Journal*, June 27, p. 1431).

The late E. Hastings Tweedy, of the Rotunda Hospital, devised an extremely simple method of elevating the pond-shaped depression which may occur in the skull of the newborn. A small nick is made in the skin over the centre of the depression, and into this is introduced the sharp tooth of one half of a single-toothed volsellum (American bullet forceps). The tooth is then gently bored through the skull bone. When penetration has been accomplished the shaft of the volsellum forceps is raised vertical to the pond, and, the tooth being now under the depression, gentle traction elevates the bone.

I have used this method, usually immediately after delivery, on all the depressed fractures I have met in the last thirty years and can endorse its simplicity and safety. It does no harm to the infants, and it saves a lot of parental anxiety.—I am, etc.,

Preston. ROBERT M. CORBET.

Treatment of Ringworm of the Scalp

SIR,—I have stated (*Journal*, May 9, p. 1052) that the use of Wood's lamp is not so vital a diagnostic aid in cases of *M. canis* scalp infections as it is in *M. audouini* cases. Therefore, argues Dr. W. A. Dewar (*Journal*, June 13, p. 1333), it appears I do not use Wood's light as a test of cure in *M. canis* ringworm—an astonishing and erroneous deduction. He will be reassured to know that the Wood's lamp is used in all cases, and I formerly wrote that "cure was assessed by negative response to Wood's light, negative result to direct microscopy, and, in one doubtful case, negative culture, all treatment having been discontinued for seven days."[1]

He informs me that I have inaccurately paraphrased his words when I quoted him as saying "the majority of authorities are in favour of *x*-ray epilation for *M. canis*." Yet, from his earlier letter (*Journal*, April 4, p. 780), there could be no misconstruing his own intention of continuing such epilation. Further experience in this field has now, more than ever, convinced me of the regularity of cure without

recourse to *x* rays in *M. canis* scalp infections. Nor has any difficulty been encountered following the return of these children to school. I have been encouraged by the receipt of letters from colleagues, including one in New Zealand, expressing their intention of giving the experiment a trial.—I am, etc.,

BERNARD A. THOMAS.

Newport, Mon.

REFERENCE

[1] Thomas, B. A., *et al.* (1945). *British Medical Journal*, 2, 346.

The Judet Operation

SIR,—Mr. J. P. Jackson (*Journal*, June 27, p. 1450) has misinterpreted my letter (*Journal*, May 23, p. 1166). I was not stating a case for the Judet operation, I was merely urging that it should not be abandoned completely in favour of displacement osteotomy. Displacement osteotomy and arthrodesis still remain, as they have been, extremely valuable procedures in the many-pronged attack on osteoarthritis.

I would agree with Mr. Jackson that the introduction of an incongruous prosthesis into a grossly arthritic joint is liable to be followed by further arthritic change, but the indication in such a case may well be for a more wide removal of the diseased tissues and not the complete abandonment of the operation. An investigation into the development of arthritis in cases of subcapital fracture of the neck of the femur, treated by the Judet method, must wait of necessity for some time. But in my experience up to now the development of osteoarthritis is less in these cases than in similar cases treated by Smith-Petersen nailing.—I am, etc.,

T. M. HENNEBRY.

London, W.1.

Post-mortem Examinations

SIR,—Dr. W. O. Pitt (*Journal*, July 4, p. 44) is not accurate in saying that the Coroners Rules, 1953, lay down that the coroner shall inform the deceased's regular medical attendant of the date, hour, and place of the post-mortem examination. Rules 4 (1 and 2b) say that the coroner shall do so, unless it is impracticable to do so, or to do so would cause the examination to be unduly delayed; this is somewhat different, and it is of interest that Dr. Pitt writes that even when the general practitioner is so informed it is "quite seldom" that he attends.—I am, etc.,

C. F. J. BARON,
H.M. Coroner for Surrey.

Leatherhead.

POINTS FROM LETTERS

Post-partum Haemorrhage

Dr. A. H. HOLMES (St. Asaph) writes: I have read the recent correspondence in the *Journal* with interest, and am particularly glad to find a general practitioner advocating the use of intravenous ergometrine for domiciliary confinements (*Journal*, June 6, p. 1278). Indeed, I should like to go further and urge all general practitioners doing midwifery to insist, so far as possible, on being called to the delivery as a routine for the express purpose of giving ergometrine by the intravenous route, and so preventing post-partum haemorrhage. The latter is one complication of labour that cannot be foretold or prevented by efficient antenatal supervision.

Medical Directory

The Editor of the *Medical Directory* writes: The accuracy of the *Directory* depends on the return of the annual schedule, which has recently been posted to members of the medical profession. Should the schedule have been mislaid I will gladly forward a duplicate upon request. The full name of the doctor should be sent for identification. As announced on the schedule, in the issue for 1954 a single alphabetical list of medical practitioners will replace the former geographical grouping of entries. Because of the extra work caused by this change, the return of all schedules as early as possible would be much appreciated. Communications should be addressed to the Editor, *Medical Directory*, 104, Gloucester Place, London, W.1.

Obituary

A. W. HARRINGTON M.D., LL.D., F.R.F.P.S.

We record with regret the death on June 7 of Professor A. W. Harrington, consulting physician to the Glasgow Royal Infirmary and Muirhead Professor of Medicine in the University of Glasgow from 1934 to 1945. He was 75 years of age.

Archibald Wilson Harrington studied medicine at the University of Glasgow, where he graduated M.B., Ch.B. in 1900, proceeding to the M.D. three years later. In 1912 he was admitted a Fellow of the Royal Faculty of Physicians and Surgeons of Glasgow and in the same year he became a member of the Association of Physicians of Great Britain and Ireland. After graduation, he held resident posts at the Glasgow Royal Infirmary, the Glasgow Royal Maternity Hospital, Coton Hill Mental Hospital, Stafford, and the Glasgow Fever Hospital. He then set up in practice at Glasgow and for two years he was clinical assistant at the Ear, Nose, and Throat Hospital. In 1906 Harrington was elected to the staff of the Glasgow Royal Infirmary, becoming assistant physician in 1913. On the outbreak of war in 1914 he entered the R.A.M.C. and in 1918 he was awarded the Serbian Order of St. Sava for his services in the Balkans theatre of the war.

After demobilization he returned to consultant practice in Glasgow and in 1925 he was appointed lecturer in clinical medicine in the University. Nine years later he succeeded the late Walter King Hunter as Muirhead Professor of Medicine, being succeeded in turn by Professor L. J. Davis, the present occupant of the Chair, in 1945, in which year he was appointed emeritus professor. His services to the University were further recognized in 1946, when the honorary degree of LL.D. was conferred upon him.

Harrington was a shy man, and until they came to know him his students found him difficult to approach. He would sometimes hide his shyness with a caustic turn of phrase, himself admitting that he was in the habit of "praising with faint damns." At the same time he was equally critical, if not more so, of his own work, possessing as he did a passion for truth and accuracy in all things. A careful observer and equipped with wide knowledge and experience of various branches of medicine, he had an almost complete understanding of his patients. He distrusted short cuts to diagnosis as potentially dangerous to the patient.

Harrington was for 38 years a member of the staff of the Glasgow Royal Infirmary, which never had a more loyal servant. Every morning he would conduct his ward rounds, and nothing was allowed to interfere with this duty. Although his health suffered as a result of his service in the war of 1914–18, it was an occasion to be noted if illness kept him away from the Infirmary; and during the period he was professor of medicine in the University he did not fail to deliver a single lecture in systematic medicine, a record of which he was particularly proud. Harrington's method of teaching was simple and clear. He practised what he preached and his students learned by his example. A perpetual student himself, he maintained his interest in the proceedings of scientific meetings up to only a few weeks before his death. Many of his residents and assistants have attained

eminence in various branches of medicine, and this in itself is a tribute to his worth as the head of a department.

His many commitments as a busy consultant and teacher did not prevent Harrington from carrying out investigations on such diverse subjects as pregnancy anaemia, cardiac infarction, and the serum treatment of pneumonia. He belonged to an age when it was possible for a man to be learned outside his own profession, and he was an avid reader, with a gift for apt quotation. He played golf and regretted he had such little leisure for fishing. Happily married, he found much comfort and peace in his home. He is survived by his widow, three sons, all members of the medical profession, and a daughter, and to them the sympathy of all their friends is extended in their loss.

A. E. EVANS, C.B.E., M.B., D.P.H.

Dr. A. Edward Evans, who died suddenly at his home in Mill Hill on June 20 at the age of 72, was well known to workers in the field of mental health not only in the British Isles but also on the Continent. He had been a Lord Chancellor's visitor in lunacy since 1938.

Albert Edward Evans received his medical education at University College Hospital, qualifying in 1907 and graduating M.B., B.S. in 1909. After holding a number of resident hospital posts he took the D.P.H. in 1910, and then became assistant medical officer at Rainhill Mental Hospital. His next appointment was that of assistant medical officer of health for Flintshire. On the outbreak of the first world war he joined the R.A.M.C. and later served in France, attaining the rank of lieutenant-colonel.

In 1914 Evans had been appointed inspector by the Board of Control—the first inspector to carry out the duties required by the Mental Deficiency Act of 1913. He returned to this post on demobilization, and in 1930 the scope of his work was widened when he was made commissioner in the Board of Control. In these two posts he had to visit the mental hospitals, private mental homes, and colonies and institutions of all kinds for the mental patient, and thus became well known to doctors and administrators in the mental health service throughout England and Wales. In 1938 he left the Board of Control when he was appointed a Lord Chancellor's visitor in lunacy. After years of most valuable service in this post, he had arranged to retire on June 30 this year. He was created C.B.E. in 1948.

During the last 20 years of his life Dr. Evans had been an ardent freemason, and lodge activities absorbed what little leisure he had. He married Dora, the daughter of the Reverend Thomas R. Rutherford. The heartfelt sympathy of all who knew him will go out to his widow.

E. O. L. writes: Possibly Dr. Evans's most distinctive service to mental health was that as secretary of study tours for the Royal Medico-Psychological Association for about fifteen years. During this period he organized a few tours to mental hospitals and mental deficiency institutions in the British Isles, but many more on the Continent—Holland, Germany, Switzerland, France, and Austria. There can be no more severe test of one's powers of organization than that of a study tour on the Continent. The chances that "something goes wrong" are innumerable. It was a task of this kind that enabled Dr. Evans to show his exceptional ability as an organizer. The thoroughness of his preparations left little or nothing to chance; he delegated tasks only to those persons upon whom he knew from experience he could rely. The doctors who were privileged to take part in these study tours can testify to the excellence of his work. The tours influenced the general trend of the work in the mental hospitals in many ways, but in two more particularly. The study tours to Holland gave a great impetus to the occupational-therapy movement in our hospitals in the early thirties, and those to Austria, Germany, and Switzerland in the later thirties did much to interest British psychiatrists in insulin shock therapy.

In many respects Dr. Evans was an exceptional personality. His quiet, courteous manner won for him readily the confidence of doctors, nurses, and patients. He seldom showed the strong hand, and used it only when he thought a patient's welfare was the issue at stake. Although he spent most of his professional career as an official visitor, he often said, "First and foremost I am a doctor, and my first loyalty is to the patient and not to any official body." His colleagues at the Board of Control and the Lord Chancellor's office can testify that while adopting this attitude, or because he adopted it, Dr. Evans gave services unique in value and in efficiency. He had a sound grasp of the clinical problems presented by mental patients, and was equally reliable when he had to deal with some administrative or legal problem, which such patients often present. With the most difficult type of patient—the paranoiac—Dr. Evans was most resourceful. These, by their suspicion, delusions of persecution, aggressive antagonism, and offensiveness, usually estrange themselves from all friends, relatives, and acquaintances; they are convinced that the whole world is against them. One such patient a few years ago told the writer, "Dr. Evans is the only doctor who has tried to understand my case." There is no greater achievement in psychiatry than to gain the co-operation of a paranoiac patient; and this Dr. Evans, by his keen insight, immeasurable patience, and great tact, achieved in several cases where others of us failed.

C. E. WALKER, D.Sc., M.R.C.S.

We record with regret the death of Dr. C. E. Walker at his home at Brighton on June 6 at the age of 81. He was at one time lecturer in histology and associate professor of cytology in the University of Liverpool.

Charles Edward Walker was born at Hove on December 9, 1871, the eldest son of Colonel E. Walker, and was educated at St. George's College, Weybridge. He studied medicine at St. George's Hospital and qualified M.R.C.S., L.R.C.P. in 1909. After qualification he held the post of assistant medical registrar at St. George's and then became demonstrator in zoology at the Royal College of Science, South Kensington, before taking up an appointment as assistant director of cancer research at Liverpool University and honorary lecturer in cytology at the Liverpool School of Tropical Medicine. In 1909 he took the Liverpool M.Sc., proceeding to the D.Sc. two years later. Soon afterwards he left Liverpool to become director of research at the Royal Cancer Hospital, Glasgow, and he remained there until the outbreak of war in 1914, when he entered the R.A.M.C. and saw service in France in 1914 and in Gallipoli, Palestine, and Egypt from 1915 to 1919. After demobilization he returned to Liverpool as lecturer in histology and associate professor of cytology, holding the joint appointment until his retirement in 1937.

Dr. Walker's original work was mainly in the fields of cytology and cancer, and his results were published largely as contributions to the *Proceedings of the Royal Society*. He also published several books dealing with the cancer problem, heredity, evolution, and cytology. Apart from his scientific publications, Dr. Walker was editor of *Shooting and Fishing on Land and Water* from 1897 to 1903, author of *Shooting and Fishing on a Small Income*, and joint author of *Self-Defence*. He attained

eminence in the sport of yachting, for in 1904 Mr. Justice Channell awarded him the Challenge Cup—the highest distinction of the Royal Cruising Club—for a single-handed cruise in his two-ton sloop *Thebe*. The following year he made another noteworthy voyage of 600 miles, an account of which is recorded in the *Journal of the Royal Cruising Club* for 1905. In those days, of course, auxiliary engines were not in general use in small boats.

His staff and students knew Dr. Walker as a kindly and courteous gentleman. His tall figure, his monocle, and his military bearing made him a notable figure in the medical school. His wife, whom he married in 1906, was the daughter of the late Mr. G. F. Meynell and widow of the late Captain A. T. England. Mrs. Walker died last year, and he is survived by a son and daughter.—N. M. H.

E. GOODWIN RAWLINSON, M.D., D.P.H.

Dr. E. G. Rawlinson, dean and director of laboratories at the Royal Institute of Public Health and Hygiene, died in London on July 4, aged 76.

Ernest Goodwin Rawlinson was born in Yorkshire and at the age of 6 accompanied his father, Marmaduke Rawlinson, with the rest of the family to Canada. He spent his boyhood there and was educated at Hartsord Collegiate School and Trinity College, Toronto University, where in 1900 he took the degrees of M.D., C.M. He always kept in touch with his old university and three years ago founded and became the first president of the United Kingdom Branch of its Alumni Association. He practised in Canada until 1903, when he came to England again and took the additional qualifications of L.R.C.P., L.R.C.S. Edinburgh, and L.R.F.P.S. Glasgow. Returning to Canada, he worked there for a further six years but finally settled in this country in 1909. In practice here until the first world war broke out, he then joined the R.A.M.C. and served for four years at home and in France. By this time he had become interested in laboratory work, with a bent towards bacteriology, and on his return to civil life he continued that study. He had seen the promise that lay in preventive medicine and did all he could to arouse interest in it and spread knowledge of it.

In 1921, after taking the diploma in public health at Oxford, he was appointed to the staff of the then Royal Institute of Public Health and became its director of bacteriology in 1922. That institute was one of the first bodies, if not the very first, in this country to provide a course of instruction for the D.P.H., and he became more and more immersed in, and devoted to, the teaching of epidemiology and kindred subjects. After the death of the founder, Sir William Smith, Rawlinson took over, under the council, pilotage of the institute.

In 1937 the Royal Institute of Public Health was amalgamated with the Institute of Hygiene under a Supplemental Royal Charter granted to the latter body, and in 1942 Rawlinson was appointed to the office of dean. Later, in 1949, he became also director of laboratories. From 1936 until the time of his death he also held the appointment of deputy medical officer of health for the metropolitan borough of Holborn.

In 1909 he married Miss Henrietta Rowson, also of Yorkshire, who survives him with their son and daughter. Their son, Dr. Peter Rawlinson, holds a public health appointment under the Government of Alberta, Canada.

We are indebted to Dr. J. W. HOUSTON for the following appreciation: Under Rawlinson the Royal Institute of Public Health and Hygiene was a most "happy ship," right down to the cabin boy. Always accessible to his students, he worked unceasingly for their benefit; nothing was too much for him, and their affection for him and their reliance on his advice and judgment were often demonstrated. He had an intense devotion to duty and even failing health during the last year did not deter him from carrying on until the last moment. When eventually preventive medicine comes into its own Rawlinson will have had a good pull on the rope by which it arrives.

Charming and unassuming, he had a most lovable personality and all the attributes of gentleness, though he could be as resolute as any occasion demanded. At the diphtheria immunization centre in Holborn, where he held a weekly clinic, he was in his element among the children. A man of taste and a talented artist, he regularly exhibited paintings and etchings at the Medical Art Society, his etchings being his own work from start to finish. He was the truest of friends and the best of company. A walk with him from Blackfriars to Greenwich among the docks and wharves where he found some of his best subjects will long live in the writer's memory.

VICTOR BONNEY, M.D., M.S., F.R.C.S., F.R.C.O.G.

A. H. L. writes: The passing of Victor Bonney will leave a void in many hearts. Others will write of his achievements in surgery and gynaecology. His colleagues on committees and councils will tell of his ability to grasp the essence of a problem and the wise judgment shown in deciding issues. As one who knew him for more than half a century I can say that he was a man of transparent honesty of purpose and action, a staunch and loyal friend who could always be relied on in an emergency. He was singularly free from jealousy, professional or otherwise, as was shown by his relations with his colleagues and especially with his senior colleague at the Middlesex, Sir Comyns Berkeley.

In the early days of our friendship he was engaged in writing the *Textbook of Gynaecological Surgery*, which was first published in 1911 under the joint names of Berkeley and Bonney. I watched him as he made all of the more than five hundred drawings that formed the principal illustrations of the book. In writing the text he was particularly careful in the choice of his words and phrases, so as to make his meaning perfectly clear and at the same time adhering to a high standard of literary English. In the last years of his life he wrote his autobiography, relating it to the London scene of his younger days and his relations with the great ones of his profession. This, together with a collection of all his contributions to gynaecology and other subjects and contemporary photographs, he placed in a box which is deposited with the Royal College of Surgeons. The contents are available to such as are interested, but the instruction is that nothing in it should be published for fifty years.

He was very anxious that the dignity of gynaecology as a surgical discipline should be fully maintained and that its practitioners should not sully its fair name by practices which departed from the high standard he had set for himself. In his treatment of his patients he was irrespective of class or colour, and he was repaid by a love and gratitude which were very remarkable. His broad humanity was an inspiration to all who knew him.

He was a great admirer of Rudyard Kipling, and knew his works almost by heart. He had written several appreciations of Kipling which show that Victor Bonney was at heart a true romantic, and in that respect he belonged more to the latter half of the nineteenth century than to the twentieth. On the artistic side he had a considerable knowledge of and love for great music and in his earlier years possessed a fine baritone voice. He was a very able draughtsman, as is evidenced by his surgical drawings, and his paintings in oil and water colour were of considerable excellence. His landscapes in particular showed a mastery of composition and of colour values.

To savour the full intellectuality of the man one had to see him in his beautiful home on the banks of the Wye, together with the charming lady his wife, to whom he was

devoted; they dispensed a gracious hospitality of the sort which is now a nostalgic memory for those of us who have lived beyond that time. There he could indulge in his favourite pursuit of salmon fishing and sketching the beautiful country around. His wife shared his early trials and labours and later, when prosperity came, fully maintained the dignity of his position. To her goes our deepest sympathy.

Dr. A. C. MOWLE, who died at his home at Devizes on May 29 at the age of 56, will be missed not only by his patients, to whom he gave devoted service, but by his fellow practitioners in Wiltshire, who, with good reason, owe much to him for his work on the Wiltshire panel and local medical committees and for the Trowbridge Division of the British Medical Association. Alfred Charles Mowle was born on October 4, 1896. From Cambridge he went on to St. Thomas's Hospital, qualifying M.R.C.S., L.R.C.P. in 1923 and taking the Cambridge M.B. two years later. After holding a resident post at the South Devon Hospital, Plymouth, he worked as a tuberculosis officer in Birmingham. From 1927 to 1931 he was chief medical officer to the Cyprus Mines Corporation, and shortly after his return to England he settled in Devizes, where he remained for the rest of his life.

Dr. A. K. JAMES writes: Dr. A. C. Mowle entered general practice in Devizes in 1933 when the late Dr. H. J. MacKay retired. He soon showed that he wished to take an active part in work outside his own practice, and he became a member of the Wiltshire Panel Committee in 1937, remaining a member of that committee and its successor, the Local Medical Committee, until his death. From 1935 to 1949 he was secretary of the Trowbridge Division, being elected chairman of the Division last year. He also represented his colleagues at the Annual Representative Meetings of the B.M.A. in 1942, 1943, and 1944. His work in all these posts was characterized by a constant efficiency, enthusiasm, and tactful understanding, and his high ideals became evident to all who had the privilege of working with him. Rather a reserved man, he gave his associates the impression that he wished to spend the major part, if not all, of his spare time in serving his colleagues to the best of his ability. It was typical of his high standards that he chose to resign the secretaryship of the Division when he found, during the discussions before and immediately after the advent of the National Health Service, that he did not share the misgivings of the majority of his colleagues, because he feared he might not be able to interpret accurately the views of the majority. The Trowbridge Division and the doctors in Wiltshire have lost a colleague who served them unselfishly for many years, and they extend to his widow and family their sincere sympathy.

Dr. D. FEARNLEY writes: Dr. Mowle's outstanding characteristic was his integrity. He followed what he saw to be right with consistency and devotion. As a colleague his sound advice was always freely available for the asking, being given from his wisdom and a practical, common-sense approach to problems, whether in medicine, medico-politics, or everyday life. As a family doctor he is remembered with gratitude and affection by his patients, to whom he brought not only his skill but also scrupulous care and whole-hearted consideration of their troubles. As a member of many committees he contributed clarity of vision, willing service, and a passionate regard for equity. He served both his patients and his colleagues to the fullness of his capacity.

We record with regret the death, as the result of a pulmonary embolism after an operation for appendicitis, of Dr. R. C. JAMESON at his home at Leeds on June 12 at the age of 82. Richard Cartwright Jameson was born at Manchester on June 4, 1871, the third son of Surgeon-General James Jameson, and was educated at Edinburgh Academy and at the University of Edinburgh, where he graduated M.B., C.M. in 1893, proceeding to the M.D. in 1910. After holding house appointments at Glasgow Royal Infirmary, Glasgow Maternity Hospital, Huddersfield Royal Infirmary, and Bradford Royal Infirmary, he decided to settle in Leeds, and was in practice there for 53 years until his final and only illness. Dr. Jameson had a well-earned reputation for being a conscientious general practitioner, and he became well known also as an ophthalmologist. In 1929, at the age of 58, he was appointed factory doctor for North Leeds, an appointment he relinquished only two years before his death.

J. E. J. writes: Dr. R. C. Jameson's death in his fifty-fourth year of general practice in Leeds will be keenly felt by his associates. Kind and gentle by nature, he was essentially a shy man of a retiring disposition, though fond of club life. He was a close friend of Moynihan, and he loved his work and lived for it. Many of the messages of sympathy on his death and tributes to his memory came from his own patients, one of whom wrote: "The doctor was one of Nature's gentlemen. We will not get another like him."

It will be with deep regret that his many friends will have heard of the death of Dr. P. W. HAMOND, who was resident in the Croydon area for nearly half a century. He died at his home at Maidstone on June 22 at the age of 73. Born at Stockport on October 6, 1879, Philip William Hamond was educated at Quernmore School in Kent and then entered Guy's Hospital Medical School. After qualifying in 1903 and holding a house appointment at Guy's, he took the London M.B. in 1904, in which year he entered general practice at Thornton Heath, Surrey, later moving to East Croydon. He quickly developed a large practice, but the work this entailed did not prevent him from taking his M.D. in 1909. After a few years he decided to take on some specialist work, and in 1917 he was appointed assistant to the V.D. clinic in Croydon, later becoming its director. In 1918 he was appointed honorary physician to Croydon General Hospital, and in 1920 assistant in the *x*-ray department, later being placed in charge of the radiodiagnostic work of the hospital. In 1926 he became physician in charge of the physiotherapy department. For many years he served both on the board of governors and on the management committee of the hospital. He was assistant secretary of the Croydon Division of the B.M.A. from 1922 to 1933; secretary of the Division from 1933 to 1937; and chairman in 1932–3. He also represented his constituency at five Annual Representative Meetings. Not only was Dr. Hamond a physician of outstanding ability and a man with a wide knowledge of many subjects, but at all times he was happy to share his knowledge with others. It was always one of his firm beliefs that general practice was an essential part of the basic training of every doctor. Of quiet disposition and sound judgment, he gave devoted service to the Croydon General Hospital for over thirty years. His final illness, coming as it did after only a few years of retirement, was borne with the philosophic attitude so characteristic of him. He leaves a widow and daughter, to whom our sympathies are extended.—S. A. F.

Dr. W. WAUGH died in Folkestone Hospital on June 25 at the age of 67 after a short illness. William Waugh was an Ulsterman from Belfast. A fine athlete as a young man, he was of international class as a Rugby player. In 1913, the year in which he qualified by taking the Irish conjoint diplomas, he was "galloper" to Sir Edward (later Lord) Carson in "Carson's Army." In the following year he settled in practice at Dover, where he remained until his death. During the first world war he served first in the Army and then as principal medical officer with the newly formed Royal Air Force at Salonika. Hard working, quick, genial, and witty, Dr. Waugh had a large practice. He was in charge of a first-aid post during the last war and probably ran more risks than when he was on active service in the war of 1914–18. He was president of the Dover Medical Society at the time of his death, and he died in harness, as he would have wished.—A. R. J.

Universities and Colleges

UNIVERSITY OF OXFORD

The following medical degrees were conferred on June 6:

D.M.—R. A. Sladden, E. M. Vaughan Williams, R. R. de Mowbray.

Dr. J. M. Walker has been elected a member of the General Board of the Faculties, by the Faculties of Medicine, Physical Sciences, Biological Sciences, Anthropology and Geography, and Agriculture and Forestry.

Professor L. J. Witts and Professor T. P. Kilner have been elected official clinical members and Dr. R. V. Coxon, Dr. G. S. Dawes, Dr. D. S. Parsons, Dr. A. G. M. Weddell, and Mr. G. J. Fraenkel ordinary members of the Board of the Faculty of Medicine. Mr. S. F. Taylor and Dr. T. C. Hunt have been elected members of the Board of the Faculty of Medicine by the General Medical Electorate.

Sir Rudolph A. Peters, F.R.S., has been elected an official member of the Board of the Faculty of Physical Sciences.

Sir Rudolph A. Peters, F.R.S., and Professor W. E. Le Gros Clark, F.R.S., have been elected official members of the Board of the Faculty of Biological Sciences.

All the above appointments are for two years from the first day of Michaelmas Term, 1953.

UNIVERSITY OF CAMBRIDGE

The following candidates have been approved at the examination indicated:

FINAL M.B.—*Part II:* [1]A. B. Aistrop, [2]I. M. Allison, [1 3]J. Anderson, [1 2]J. D. Avison, [4]A. J. F. Barratt, [1 2]S. G. Bayliss, [1 2 3]D. W. Bentinck, [1 2]Mrs. A. B. Bentinck Speed, [2]L. J. Bishop, [1 3]D. B. Bower, [1 3]T. C. Bradford, [2]L. F. Brunt, [2]N. P. Burns, [1 2]L. R. L. Burton, [1 2 3]R. M. Butcher, [2]V. G. Caiger, [1 3]D. Campbell, [3]W. H. Carling, [1 2 3]J. B. Carver, [1]R. H. Champion, [1 2 3]J. M. Clifford, [1 2 3]G. M. Cochrane, [1 2]J. Cocker, [1]C. W. M. Cooper, [1 2]D. E. Corlett, [1]D. W. Couch, [1]K. Coventry, [1 2 3]H. F. Cowper Johnson, [1]F. S. Cozens, [1 2 3]E. J. Cretney, [1 3]J. C. B. Daman, [2]R. J. Daniels, [1 2 3]D. M. Davies, [1]E. R. Davies, [1]A. E. L. de Thierry, [1 3]J. P. Dickson, [1 2 3]A. H. Dimond, [1 3]D. G. Dingle, [3]P. F. Dixon, [1 2 3]P. M. E. Dutton, [2 3]B. I. F. Eminson, [1]J. P. English, [1]J. P. F. C. Evans, [1 2 3]B. E. Farnham, [1 3]J. R. T. Finlayson, [1 3]M. V. J. Fitzgerald, [1]J. M. Fitzsimons, [1]J. T. Fitzsimons, [1 2 3]M. G. A. Forrest, [1 2 3]R. Gardner, [2 3]R. H. Gibbon, [1 3]J. T. Gibbs, [1 2 3]J. E. Goodess, [1 2 3]D. N. M. Goodson, [1]B. G. Gradwell, [1]G. McC. Gransden, [3]Mrs. M. H. P. Gregory, [1 3]M. C. Guard, [1]P. M. Hacking, [1 2 3]R. W. Hall, [1]J. W. Harding, [1 2 3]M. B. Harris, [1]P. W. Hayward, [1 2 3]W. B. Hepburn, [1 2 3]M. Heslop, [1]F. Heyes, [1]M. B. Heywood-Waddington, [2]A. F. Hignell, [3]C. B. Hobbs, [1 2 3]H. J. Hodgson, [3]J. A. Holland, [2 3]B. Holt, [1]M. Horowitz, [1]S. M. Houghton, [1 2 3]R. Hutchinson, [1]R. J. Hutchinson, [1]H. R. M. Johnson, [1]B. P. Jones, [2 3]P. O. Jones, [1]R. V. Jones, [1 2 3]R. V. H. Jones, [2]A. McL. Keil, [1]A. J. Kenmuir-Evans, [3]F. E. Kenyon, [1 2 3]Mrs. E. S. Kerr, [1]E. O'G. Kirwan, [1 2 3]A. R. Kittermaster, [1 2]R. J. Knight, [1 2 3]R. J. W. Lambert, [1 2 3]J. E. Lennard-Jones, [2]I. Lenox-Smith, [1]D. G. Lethem, [2]H. E. D. Lloyd, [2]J. S. Lloyd, [1 2]S. P. Lock, [1]I. B. Lyon, [1 2 3]W. O. McCormick, [1 2 3]J. A. McEwan, [1 2]C. M. McGregor, [1 2 3]N. D. Mackichan, [2]Mrs. J. F. Mackworth, [1 2 3]A. F. Madge, [1 2 3]I. M. J. Mair, [1]A. C. Markland, [1]H. C. Masheter, [1 2 3]P. M. O. Massey, [1]B. A. Maurice, [1 3]G. F. Mayall, [1 2 3]G. Meachim, [1 2 3]R. A. Miley, [1 3]E. J. Mitchell, [1 2 3]D. G. Montefiore, [1]A. B. Myles, [1]M. J. Mynott, [2 3]J. C. Newell Price, [1 3]K. R. Oliver, [1 3]I. Oswald, [1 2 3]J. Paterson, [1 2 3]G. N. Penlington, [1]H. G. Penman, [1]M. J. W. Penn, [1 2]J. G. Pritchard, [1]M. J. Pritchard, [1]P. H. Pullen, [1 2]M. J. Purves, [3]G. A. Reed, [1]I. R. D. Reid, [1 3]D. K. Robinson, [1]R. Routledge, [1 2 3]R. A. Roxburgh, [1 2]J. D. Salmon, [1 2]E. S. J. Samuel, [2]J. R. Scott, [1]R. J. Sellick, [1]G. D. H. Shephard, [1 2 3]P. Sleight, [1 2 3]I. M. P. Smeed, [1 2]P. T. Smith, [1 3]J. K. Snell, [1 2 3]J. L. Stevens, [1 2]I. G. Tait, [1 2]J. L. Tasker, [1]M. B. Teal, [1 2]H. T. Thomas, [1]A. D. Thursz, [1 2 3]J. E. C. Tower, [1]M. Trede, [1 3]D. E. Tunnadine, [1 2 3]T. M. Vanier, [1 2]G. P. Vaughan, [1]R. J. Vaughan, [1 3]J. D. S. Vernon, [1 2 3]P. C. Vivian, [1 2 3]E. H. M. Walker, [1 2 3]R. K. Waterhouse, [1 2]J. H. H. Webster, [1 2 3]P. Wellings, [1 2]P. D. W. Wickenden, [1 2]L. Wilkinson, [1 2 3]E. D. Williams, [1]R. V. F. Williams, [1 2 3]G. C. E. Wilson, [3]H. J. Wood, [1 3]J. R. Wood, [2]M. T. C. Wright, [1 2 3]C. M. Yates, [1]N. W. H. Young. Old Regulations: [2 3]J. C. S. Turner. *Part I (Pathology and Pharmacology):* A. B. Aistrop, R. C. Benians, G. F. B. Birdwood, N. V. D. Bunker, R. M. Butcher, D. J. Buttery, R. H. Champion, M. J. Clarke-Williams, C. W. M. Cooper, D. W. Couch, K. Coventry, E. J. Cretney, J. Crook, J. C. B. Daman, R. J. Daniels, Mrs. E. J. P. Davies, E. R. Davies, J. P. Dickson, A. H. Dimond, J. A. Dryden, P. M. Dunn, P. M. E. Dutton, Mrs. E. A. Eldon, J. P. F. C. Evans, J. M. Fitzsimons, J. E. Goodess, P. Gortvai, P. M. Hacking, R. W. Hall, M. B. Harris, P. W. Hayward, M. B. Heywood-Waddington, S. M. Houghton, H. Jacobs, H. R. M. Johnson, B. P. Jones, R. V. Jones, R. V. H. Jones, A. J. Kenmuir-Evans, F. E. Kenyon, E. O'G. Kirwan, A. R. Kittermaster, S. R. Laing, R. C. Lawson, E. K. Lee, D. G. Lethem, J. C. Lindsay, H. E. D. Lloyd, I. B. Lyon, W. O. McCormick, A. C. Markland, H. C. Masheter, P. M. O. Massey, B. A. Maurice, J. M. Mennell, M. T. Moore, E. Moran, R. H. Morgan, A. B. Myles, M. J. Mynott, R. C. Nainby-Luxmoore, G. G. K. Parsons, H. G. Penman, A. T. Porritt, M. J. Pritchard, P. H. Pullen, E. S. Reed, G. A. Reed, I. R. D. Reid, J. D. Salmon, E. S. J. Samuel, R. J. Sellick, G. D. H. Shephard, F. R. Spink, N. A. Subedar, M. B. Teal, A. D. Thursz, S. A. Tillyard, J. E. C. Tower, M. Trede, D. E. Tunnadine, R. J. Vaughan, R. J. Vince, L. Weiss, P. D. W. Wickenden, L. Wilkinson, W. D. W. Williams, H. J. Wood, J. R. Wood, C. M. Yates.

[1]Passed in principles and practice of physic. [2]Passed in surgery. [3]Passed in midwifery and gynaecology.

UNIVERSITY OF GLASGOW

The following diplomas were awarded on June 10:

D.P.H.—G. G. Browning, Helen W. Greenlees, H. M. Macfarlane, Sheenah J. McK. Russell, L. G. Samuel, R. Short, R. S. Sloan, Elizabeth Stewart, and N. Watson.

UNIVERSITY OF LONDON

The following candidates have been approved at the examination indicated:

ACADEMIC POSTGRADUATE DIPLOMA IN PSYCHOLOGICAL MEDICINE.—*Part I:* J. E. A. Bartlet, Valerie A. Cowie, L. A. Hersov, S. G. E. Laverty, I. J. MacDonald, A. A. Reid, M. J. Rosenthall.

The following candidates have been approved at the examination indicated:

THIRD M.B., B.S.—[1 4]J. H. Bulmer, [1 4]R. Y. Calne, [1 4]A. F. Champion, [1 4]M. L. Crosfill, [1 4]M. J. Hodgson, [1 2]H. F. Jeejeebhoy, [1 4]B. S. Jones, [1 5]P. Knipe, [1 5]Caroline S. Koblenzer, [1 4 5]P. Mestitz (University Medal), [1 5]J. L. Turk, [1 4]T. H. M. Warburton, [1 4]R. S. Williams, [1 4]D. A. H. Yates, Jessamine M. Akhurst, D. P. Adamson, B. L. Anderson, Margaret L. Arden, Janet E. Arnott, J. F. Arthur, K. J. Atkins, Bridget K. Attlee, N. J. Badham, Jean F. Baker, Patricia M. Banks, A. R. Barber, C. J. Barlow, M. J. Barnard, Joyce Barnett, A. F. Barrett, B. A. J. Barrow, J. L. Barton, D. A. V. Bearblock, A. R. Bearn, D. P. Beck, Yvonne G. Beeching, Mary A. M. Beeney, J. S. Bennett, F. E. Bennetts, R. Benson, E. G. A. Bernez, P. B. Biddell, G. C. Bird, I. C. Black, N. A. Black, A. G. Boag, Anne Booth, R. T. Booth, P. D. Bowen, W M. S. Boyd, Ann N. Bradford, J. J. Bradley, Margaret H. Bradshaw, Cynthia I. Breillat, Eileen M. Briant, E. R. Briant, B. J. Brook, E. F. Brooks, Irene P. Brown, Jean Brown, Joan T. Bruce, Barbara J. Bruce Low, Jennifer T. Bryant, E. A. C. Buckell, J. S. Bunting, Vivien Burn, J. D. Bury, Katherine M. Cadbury, Ailleen M. Caldwell, C. D. Campbell, Pamela F. Carter Braine, Elizabeth O. Castell, R. A. Cawson, D. R. Chase, Chia Ah Kwan, R. G. Chitham, Gillian M. Churcher, D. L. Clarke, D. J. A. Clarke, P. Cliffe, Mary Clothier, P. Cook, D. C. Cornish, Kathleen D. F. Corti, Violet G. Cousins, Gerda J. Crow, G. Currie, Agnes M. S. Curry, P. J. Dally, B. L. P. Dalton, R. Danbury, Helen M. Danziger, Shirley F. Dauncey, A. P. Davies, Francis Ll. Davies, G. Davies, D. A. de Renzy-Martin, A. G. F. Dominick, F. de S. Donnan, B. W. Duck, D. V. Duckworth, G. W. Duckworth, P. G. Dunbar, G. T. Dunger, Sylvia Dunn, J. V. Dyer, L. W. Eldon, Lindsay M. Elliott, Mary A. Elsdale, Jean A. Evans, J. Ll. Evans, Jean A. Fairhurst, J. K. Fanning, R. H. Farrell, C. P. Farthing, P. L. Fieldus, J. Fisher, Margaret Fisher, A. Fletcher, Sheila M. Forbes, W. A. Forrest, B. Fox, Phillida M. Frost, I. C. Fuller, Gillian Gandy, D. C. Gardner, A. P. Garland, Katharine R. Garrett, R. E. M. Geldart, K. W. Giles, M. C. Glassett, R. B. Glover, D. H. Glyn, R. M. Goddard, H. R. Gompertz, Margaret C. Gorrill, Daphne F. Grainger, V. A. Grantham, J. M. Gray, M. Greenberg, A. H. Gretton, A. J. G. Griffin, T. P. Griffith, R. M. Griffiths, W. L. Griffiths, Valérie A. E. Guex, J. A. Gumbrell, I E. Gurner, J. M. S. Hague, M. I. Hale, Judith M. Hall, S. A. Hall, T. E. Hall, V. T. Hammond, Dorothy E. Harris, D. Harvey, S. K. Heywood, J. B. Hickling, D. A. Hill, G. G. Hill, M. C. Hill, D. Hines, Natalie J. Holloway, G. W. Holmes, E. T. R. Holt, Blanche M. Hooper, J. S. Hopkins, E. C. Howarth, M. M. Husainee, D. S. Hutton, J. R. F. Ingall, H. P. H. Ivens, R. James, J. C. Jelleyman, J. A. Jemson, A. H. John, M. Johnstone, Vivian K. Jones,

Nancy Kaan, C. G. Keith, K. Kelly, A. B. Kennard, P. A. H. King, Sheila M. King, P. J. W. Knell, S. M. Lacey, L. Langdon-Herring, P. T. Lascelles, J. O. N. Lawson, Lesley P. Leader, M. Leahy, P. Lebon, Lee Lian-Heng, J. Le Gassicke, E. R. Lester, Barbara Lewis, E. C. Lewis, Agnes D. F. Lodhi-Hyder, T. A. E. C. Lorenzen, P. Los, R. E. Lovelace, Margaret F. Lowe, M. M. Lubin, D. F. Lunn, A. G. McCallum, Margaret R. McDonald, Patricia McDonald, E. N. McKenzie, M. B. McKerrow, Dorothy M. McWhirter, D. H. Marjot, G. Matthews, D. Mattingly, P. G. Mellett, M. H. Mercer, D. G. Millard, J. S. Miller, D. B. Moffat, Mary Moffatt, G. L. Money, I. A. Moollan, A. Moore, P. B. Moorhead, D. T. G. Morgan, Patricia E. Mortimer, R. F. Morton, R. J. Mules, L. R. Mundy, Lilias M. A. Munro, M. A. Ness, R. G. D. Newill, C. G. H. Newman, J. Nickson, Norma H. W. Noakes, J. S. Noaks, J. S. Norell, Jean M. North, M. P. O'Dwyer, J. S. Ogilvie, Gillian Oliver, L. C. Oliver, P. J. Olney, Elizabeth S. Ordish, Pamela M. Ordish C. S. Osen, Nancy M. Page, R. B. Parker, D. F. Parkin, J. J. Parry, Helen L. M. Partridge, I. S. Paterson, Iris O. Peachey, D. E. Pearsons, C. M. H. Pedler, Elizabeth L. M. Perkins, J. F. Perren, B.Ll. C. Phillips, R. M. Phillips, L. A. Pike, E. M. Pilkington, R. G. Pledger, R. W. Plowright, P. B. Poole, C. J. Porteous, M. F. Porter, O. H. D. Portsmouth, Rosemary D. Prior, J. D. Pryce, M. A. Pugh, A. I. Rae, P. J. Rawlinson, R. D. H. Reddy, P. I. Reed, N. D. Reis, C. H. J. Rey, J. W. Richardson, D. Ricketts, C. C. Riley, Brenda K. Rimmer, G. D. Ripley, T. M. F. Roberts, O. W. Robinson, S. B. Rosalki, Vera Rose, Annette B. Rosenkranz, R. G. Rowe, A. D. Rowlands, J. A. C. Rozario, Aileen M. Ryan, H. S. S. Ryan, N. R. Sales, Dorothy Sanderson, E. C. Scanlon, J. A. Scanlon, K. Scott, S. C. C. Scott, F. G. M. Seager, Muriel J. Seaman, Patricia M. Searle, P. H. Setna, R. J. Sharland, Joan P. V. Shaw, C. S. Sheldon, S. Shere, R. Shorter, E. Silverstone, Elizabeth A. Smith, Mary N. Smith, M. G. Smith, Sylvia F. R. Smith, J. T. Smyth, B. A. Southgate, P. E. Spalding, F. G. H. Spicer, M. T. Stather-Dunne, Mary K. Stedman, T. B. Stephen, J. W. Stephenson, Hilda J. Stevens, Phyllis A. Stevens, V. W. Steward, P. B. Storey, V. C. Storey, R. Stowe, M. K. Strelling, D. Stuart, B. D. Thomas, D. H. C. Thomas, D. K. MacM. Thomas, D. Thomas, H. M. Thomas, Patricia I. Thomas, Heather B. Thompson, Diana J. Thuell, Janet C. Tonge, A. H. Tooley, J. B. Tucker, B. A. Tudgay, Lesley P. D. Tunnadine, Margaret I. Upton, P. J. Verrill, G. R. Vesey, C. M. Vickery, C. T. Vincent, G. D. Vinden, M. T. Wade, G. S. Wakefield, Maire P. Wallington, Patricia G. Wallis, Margaret P. Watson, H. R. Watson-Baker, A. N. E. Watt, Marjorie E. Watts, J. L. Weeks, P. K. Wheatley, Elizabeth P. Wheaton, B. R. Whittard, Jean B. Wickings, J. J. Williams, Margaret S. I. Williams, Myrtle L. Williams, T. C. G. Williams, M. S. Wilson, Shelagh R. Wimhurst, A. G. Winfield, A. R. Winrow, Rosemary J. Wisdom, A. E. Wood, Cynthia Wright, H. A. Yerbury, J. R. Young, K. J. Zilkha.

[1]With honours. [2]Distinguished in pathology. [3]Distinguished in medicine. [4]Distinguished in applied pharmacology and therapeutics. [5]Distinguished in surgery. [6]Distinguished in obstetrics and gynaecology.

UNIVERSITY OF WALES

In Congregation on July 17 a number of honorary degrees were conferred, including that of LL.D. on Dr. Edgar Douglas Adrian, O.M., in recognition of his eminence as President of the Royal Society and for his great distinction in the field of physiological studies; on Sir Walter Russell Brain as President of the Royal College of Physicians of London and for his distinction as a physician; on Sir William Wilson Jameson for his great services to public health in his former position as Chief Medical Officer to the Ministry of Health and the Ministry of Education; on Professor Robert Frederick Loeb in recognition of his eminence as a physician and teacher of medicine in the United States of America; on Dr. Patrick Theodore Joseph O'Farrell as the holder of the high office of President of the British Medical Association in 1952–3 and for his services to medicine; on Professor Wilder Graves Penfield, O.M., for his outstanding contributions to the advancement of knowledge and practice in the field of neurosurgery and neurology; on Sir Clement Price Thomas in recognition of his great distinction as a thoracic surgeon and for his contributions to the advancement of surgical knowledge and practice; and on Professor Arvid Wallgren in recognition of his distinction as a teacher of medicine and his contributions to the study of child health.

The following candidates at the Welsh National School of Medicine have satisfied the examiners at the examination indicated:

EXAMINATION FOR THE TUBERCULOUS DISEASES DIPLOMA.—R. J. B. Anderson, A. Aziz, J. J. Griffiths, M. B. Hoda, H. V. Venkataramaniah, S. J. Hubert, R. D. Maclean, Cathleen Monaghan, Y. Rajasekhar, K. R. Setty, T. D. Sivalingam, V. Visweswariah, K. D. Young.

ROYAL COLLEGE OF SURGEONS OF ENGLAND

At a meeting of the Council of the College held on June 11, with Sir Cecil Wakeley, President, in the chair, the following were co-opted to the Council for the year 1953–4 representing the various branches of practice indicated in parentheses: Dr. O. C. Carter (general practice); Professor A. M. Claye (gynaecology and obstetrics); Mr. M. L. Formby (otolaryngology); Dr. B. R. M. Johnson (anaesthetics); Mr. A. B. Nutt (ophthalmology); and Sir William Kelsey Fry (dental surgery).

Mr. R. Danbury (Royal Free) was presented with the Begley Prize.

Fellowships

Diplomas of Fellowship were granted to the following successful candidates: R. L. Rees, D. G. B. Bennett, R. A. J. Baily, R. L. A. Gouges-d'Agincourt, J. R. Dyer, R. L. Batten, J. G. Kendall, R. Pracy, G. Mizbah, R. W. Povey, A. H. M. Littlewood, C. S. Kirkham, C. F. Noon, D. B. Leaming, P. W. Seargeant, D. C. Stevenson, E. C. Edwards, Phyllis A. George, D. B. J. Wardle, F. G. Ellis, E. A. Badoe, F. M. Khan, I. B. Speight, B. Cohen, B. M. Chatterjee, A. K. Barat, R. D. Venn, K. J. M. Watson, W. G. Davidson, P. C. Ghosh, E. O. Williams, D. S. Kidd, W. P. Crone, R. Ger, J. R. Kenyon, F. D. Martinson, J. P. Swain, W. N. Coombes, J. S. Groves, J. M. Mynors, Daphne M. Scott, J. Swartz, H. T. Thompson, P. Abbey, H. H. Francis, Irene D. R. Gregory, E. F. Shanahan, N. D. Ashe, H. J. Bagnall, R. J. Bennett, R. P. Chakrabarty, M. W. Falloon, J. M. Hay, R. Jacobs, A. Kelly, L. E. Neri, J. N. Ravalia, E. L. Angliss, J.-J. Brossy, J. V. L. Colman, D. F. Cossar, D. G. L. Davies, R. F. Elliott, D. J. Ghadialy, J. K. Henderson, A. F. Hunter, P. O'Donoghue, O. E. Owen, I. W. Payne, P. Rhodes, V. K. Vani, A. J. C. Allison, J. K. Clarebrough, R. H. L. Ferguson, H. J. Groves, P. J. Heery, J. Jaconelli, G. Slaney, G. C. Slee, J. G. Watson, M. E. E. White, I. A. Agjee, N. R. Amesur, M. I. K. Anwar, G. B. Cavaye, S. K. Chatterjee, J. A. Hanley, C. Q. Henriques, J. T. Hueston, G. J. Kane, P. A. King, E. R. McKenzie, C. P. Mills, J. K. M. Quartey, M. W. Reece, N. A. Stephens, C. H. Talbot, A. W. R. Williamson, R. E. Candlin, D. S. Cole, K. J. Coleman, R. D. Cundall, M. B. O'Donnell, D. A. Simpson, R. H. Thorlakson, W. J. D. Bradfield, B. S. Pearson, R. J. M. Whittle.

Membership

Diplomas of Membership were granted to G. P. Lowther (Bristol) and B. K. A. Muller (Ceylon).

Hospitals were recognized under paragraph 23 of the F.R.C.S. regulations as follows: Tindal General Hospital, Aylesbury, *paragraph 23c*, ear, nose, and throat house surgeon. Amersham General Hospital, *from January, 1954*, casualty officer. Horton General Hospital, Banbury, *from January, 1954*, casualty officer (senior house officer). Blackburn and East Lancs Royal Infirmary, *paragraph 23c*, senior house officer; *revision*, house officer, both ear, nose, and throat department. Royal Infirmary, Bradford, *additional recognition*, two house officers (general surgery and urology) for six months. Brighton General Hospital, *revision to read as follows*, surgical registrar (for 12 months); house surgeon (general), and senior house officer (orthopaedic surgery), both for six months. Royal Sussex County Hospital, Brighton, *additional recognition*, registrar (general surgery), and registrar (orthopaedic surgery), both for 12 months; reduction from twelve to six months period of recognition of first, second, and third house surgeons. Bury General Hospital, *additional recognition*, senior house officer (surgical) for six months; *from January, 1954*, senior house officer (orthopaedic) to be recognized for casualty training and not, as hitherto, for general surgery. Hove General Hospital, resident surgical officer (senior house officer) (general surgery) for six months; *from January, 1954*, casualty house officer. Royal Lancaster Infirmary, *revision to read as follows*, senior house officer (surgical); house surgeon; orthopaedic house surgeon, all for six months. St. James's Hospital, Leeds, *additional recognition*, third house surgeon; registrar (orthopaedic); senior house officer (orthopaedic), all for six months. Lewisham Hospital, London, *from January, 1954*, two casualty officers; *additional recognition*, orthopaedic registrar for 12 months. St. John's Hospital, London, *from January, 1954*, casualty officer. Mildmay Mission Hospital, London, *from January, 1954*, casualty officer. Ancoats Hospital, Manchester, *revision to read as follows*, surgical registrar for 12 months; senior house officer (assistant resident surgical officer); two junior house officers (general); junior house officer (orthopaedic), all for six months; *from January, 1954*, resident casualty officer (senior house officer). Nottingham General Hospital, *from January, 1954*, two casualty officers. South Devon and East Cornwall Hospital, Plymouth, *revision to read as follows, Greenbank Road*: resident surgical officer, first, second, and third house surgeons, all for six months; *from January, 1954*, casualty

officer; *Devonport*: senior house surgeon; house surgeon, both for six months; *Freedom Fields*: senior house officer (surgical); two house surgeons, all for six months; *from January, 1954*, casualty officer. St. Mary's Hospital, Portsmouth, *additional recognition*, third house surgeon for six months; *from January, 1954*, casualty officer (senior house officer); the hospital is recognized temporarily until December 31, so that the whole position must be reviewed before that date. Swindon Victoria Hospital, *confirmation of temporary recognition*, surgical registrar for 12 months; two house surgeons for six months. Great Western Hospital, Swindon, *from January, 1954*, two resident casualty officers. Odstock Plastic and Oral Surgery Centre, Salisbury, registrar and house officer, both for six months. Salisbury General Hospital, *from January, 1954*, casualty officer. Weston-super-Mare General Hospital, resident surgical officer for six months. Worthing Hospital, revision, increased from six to twelve months in period of recognition of resident surgical officer; *from January, 1954*, casualty officer.

ROYAL COLLEGE OF PHYSICIANS OF IRELAND

The following Members were admitted to the Fellowship of the College on June 5: G. Gregg, R. H. O'Hanlon, R. W. M. Strain, and P. J. Sweeney. Admitted *in absentia*, W. D. Hughes and Muhammad Aslam Pirzada.

On the same date the following were admitted to the Membership: J. P. A. Ryan and J. D. Sullivan.

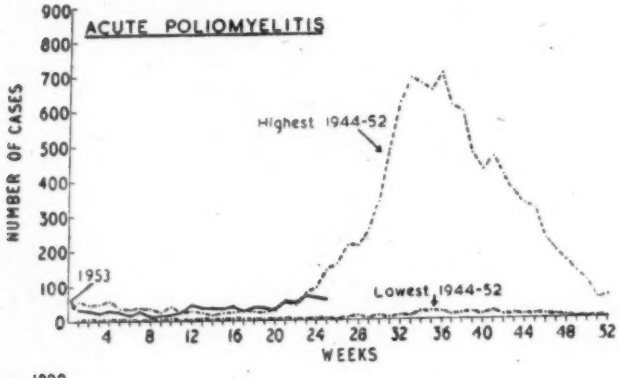
FACULTY OF RADIOLOGISTS

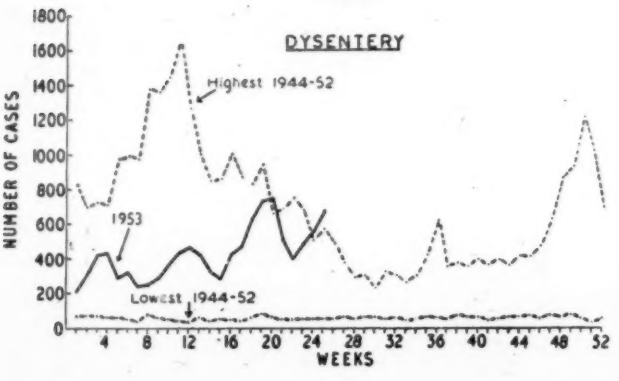
At the examination for the Fellowship of the Faculty of Radiologists held in April, 1953, the following satisfied the examiners: *Radiodiagnosis*, D. Lloyd Dick, D. E. Fletcher, P. F. New, J. N. Pattinson, E. G. Redman, T. R. Riley, D. Stenhouse, J. Sutcliffe, D. Sutton, and C. K. Warrick. *Radiotherapy*, J. Boland, W. B. Dawson, Mary Douglas, and J. A. Orr.

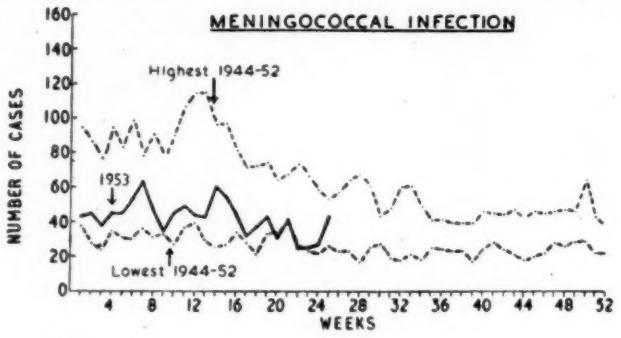
Vital Statistics

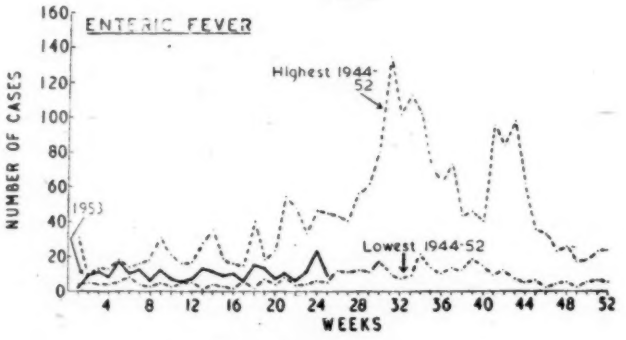
Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported in each week during the nine years 1944–52 are shown thus - - - - - - -, the figures for 1953 thus ———. Except for the curves showing notifications in 1953, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.









Infectious Diseases

The largest fluctuations in the trends of infectious diseases in England and Wales during the week ending June 27 were a decrease of 709 for measles, from 7,580 to 6,871, and increases of 119 for dysentery, from 557 to 676, and 110 for scarlet fever, from 1,223 to 1,333.

The largest falls in the number of notifications of measles were 241 in Lancashire, from 1,551 to 1,310; 118 in London, from 291 to 173; and 109 in Shropshire, from 159 to 50; and the largest rises were 82 in Cornwall, from 141 to 223; and 68 in Somersetshire, from 165 to 233. The variations in the local trends of scarlet fever were small; the largest was an increase of only 23 in Essex, from 64 to 87. 4,116 cases of whooping-cough were notified, 12 more than in the preceding week. The largest rise was 39 in Surrey, from 104 to 143, and the largest fall was 40 in Essex, from 328 to 288. 18 cases of diphtheria were notified, 7 fewer than in the preceding week. The largest return for diphtheria was 3 in Plymouth C.B.

60 cases of acute poliomyelitis were notified. These cases were 5 more for paralytic and 10 fewer for non-paralytic than in the preceding week. The largest returns were Kent 7 (Margate M.B. 2, Romsey and Stockbridge R.D. 2); Wiltshire 5 (Salisbury M.B. 3, Pewsey R.D. 2); London 4; Middlesex 4 (Harrow U.D. 2); Southampton County 4 (Bournemouth C.B. 2); Sussex 4 (Worthing R.D. 2).

The largest centres of dysentery were London 135 (Paddington 18, Finsbury 14, Deptford 13, Islington 13); Lancashire 86 (Liverpool C.B. 25, Preston C.B. 17, Oldham C.B. 13, Manchester C.B. 10); Bedfordshire 55 (Luton M.B. 49); Middlesex 54 (Willesden M.B. 10); Yorkshire West Riding 50 (Wakefield C.B. 24, Leeds C.B. 10); Norfolk 42 (Blofield and Flegg R.D. 17, Kings Lynn M.B. 12); Durham 34 (Stanley U.D. 25); Surrey 26; Nottinghamshire 20 (Arnold U.D. 17). The incidence of dysentery has been relatively high in Scotland, where 2,195 cases were notified in the first twenty-two weeks of this year; of these, 905 were notified in Glasgow and 331 in Edinburgh.

291 of the 505 cases of food-poisoning were notified in Lancashire; these cases were spread through 31 areas.

Week Ending July 4

The notifications of infectious diseases in England and Wales during the week included scarlet fever 1,066, whooping-cough 4,690, diphtheria 14, measles 6,610, acute poliomyelitis 126, dysentery 476, paratyphoid fever 3, and typhoid fever 1.

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending **June 27** (No. 25) and corresponding week 1952.

Figures of *cases* are for the countries shown and London administrative county. Figures of *deaths* and *births* are for the 160 great towns in England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES in Countries and London	1953 Eng. & Wales	1953 Lond.	1953 Scot.	1953 N. Ire.	1953 Eire	1952 Eng. & Wales	1952 Lond.	1952 Scot.	1952 N. Ire.	1952 Eire
Diphtheria	18	0	12	2	0	23	2	2	0	
Dysentery	676	135	147	4	1	145	34	77	90	3
Encephalitis, acute	2	0	0	0		4	0	1	0	
Enteric fever:										
Typhoid	4	1	0	0	0	6	0	0	1	
Paratyphoid	5	0	5(B)	0	0	38	0	5(B)	0	1 (B)
Food-poisoning	505			8		104	8		1	
Infective enteritis or diarrhoea under 2 years				22	18				19	30
Measles*	6,871	173	239	267	102	6,285	639	246	223	392
Meningococcal infection	43	4	17	0	2	33	3	17	0	1
Ophthalmia neonatorum	31	2	11	0		38	5	5	0	
Pneumonia†	328	16	143	5		383	24	158	2	
Poliomyelitis, acute:										
Paralytic	49	2	4	6	2	49	6	7	5	1
Non-paralytic	11	2				19	1			
Puerperal fever§	324	33	13	4	0	269	40	17	2	
Scarlet fever	1,333	87	187	52	18	1,068	99	179	10	58
Tuberculosis:										
Respiratory			144	29				143	27	
Non-respiratory			36	6				27	5	
Whooping-cough	4,116	349	394	49	47	2,573	105	153	63	130

DEATHS in Great Towns	1953 Eng. & Wales	1953 Lond.	1953 Scot.	1953 N. Ire.	1953 Eire	1952 Eng. & Wales	1952 Lond.	1952 Scot.	1952 N. Ire.	1952 Eire
Diphtheria	0	0	0		0	0	0		0	0
Dysentery	3	0				1	0		0	
Encephalitis, acute		0			0		0			0
Enteric fever	0	0	0			1	0		0	
Infective enteritis or diarrhoea under 2 years	8	0	4	0	1	3		2	3	3
Influenza	6	0	1	0	2	3	1		0	0
Measles		0	0		1		0		0	1
Meningococcal infection		1	0				0			
Pneumonia	138	20	13	11	4	135	28		6	2
Poliomyelitis, acute	2	0			0	1	0			0
Scarlet fever		0	0		0		0		0	0
Tuberculosis:										
Respiratory	90	11	12	1	10	114	16	17	2	8
Non-respiratory		1	3	0	2		4	4	0	1
Whooping-cough	2	0	2	0	0	1	0		0	1
Deaths 0–1 year	233	28	37	9	12	187	31	29	11	14
Deaths (excluding stillbirths)	4,619	657	508		147	4,235	604	483	104	176
LIVE BIRTHS	7,951	1232	879	235	368	7,579	1203	913	234	440
STILLBIRTHS	211	19	28			164	13	25		

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
§ Includes puerperal pyrexia.

Medical News

American Surgeons to Meet in London.—The American College of Surgeons has accepted an invitation from leading surgeons in England to hold a Sectional Meeting in London next year. The meeting will be from May 17 to 19. It will be immediately preceded by the annual meeting in Leeds of the Association of Surgeons of Great Britain and Ireland (May 13 to 15), and be followed by special sessions of the International Society of Surgery in Paris. British members of the Arrangements Committee for the meeting include Sir Cecil Wakeley, P.R.C.S. (chairman), Mr. A. Lawrence Abel, Sir Stewart Duke-Elder, Sir Gordon Gordon-Taylor, and Professor Lambert Rogers. This will be the first occasion since 1914 that a sectional meeting of the American College of Surgeons has been held in London.

Anonymous Donation to College of Surgeons.—After the meeting of the council of the Royal College of Surgeons on July 9 the following statement was issued by the College: The task of the College in the training of young surgeons from the Commonwealth, and the policy recently adopted of reciprocal training and education in the Empire, especially with the Royal Australasian College of Surgeons, were recognized in an anonymous donation of £100,000, of which £75,000 is to be devoted to the new research laboratories and lecture halls of the College in London, and £25,000 to the Royal Australian College of Surgeons for the development of its educational work.

British Association of Urological Surgeons.—The ninth annual meeting of the British Association of Urological Surgeons was held in Leeds from June 25 to 28, under the presidency of Mr. E. W. Riches.

The following were elected officers and members of Council for 1953–4: *president*, Mr. T. J. Millin; *vice-president*, Mr. R. H. O. B. Robinson; *honorary secretary*, Mr. A. W. Badenoch; *honorary treasurer*, Mr. R. H. O. B. Robinson; *honorary editorial secretary*, Mr. J. D. Fergusson; *members of council*, Mr. J. C. Anderson, Mr. David Band, Mr. T. L. Chapman, Professor V. Dix, Mr. H. G. Hanley, Mr. Arthur Jacobs, Mr. J. G. Sandrey, Mr. H. Hamilton Stewart. The scientific discussions will be reported in the *British Journal of Urology*.

Child Adoption.—The Standing Conference of Societies Registered for Adoption has issued a useful pamphlet, called "Child Adoption," for those considering this step. Besides giving practical information on how to make an adoption, the pamphlet discusses some of the factors which make for success or failure. The advice is much to the point: "Remember that in this country adoption is for life," "Adopting a baby does not help to keep a marriage off the rocks," "It is not a good thing to adopt a child because of fear of pregnancy or to avoid the risks of childbirth." The legal side is clearly explained and the question of telling the child about his adoption is dealt with: "The time to tell a child is as soon as he is able to talk to you." The pamphlet ends with a complete list of the registered adoption societies in England and Wales. It will be an invaluable guide to anyone concerned with the adoption of a child. Copies may be obtained, price 9d. (1s. postage free), from the hon. secretary of the Standing Conference, Gort Lodge, Petersham, Surrey.

Pre-Registration Certificates.—Hospital authorities have now received the forms for certifying the satisfactory completion of a pre-registration resident appointment. Details must be given of the nature and duration of the appointment, and a member of the consultant or specialist staff under whom the applicant has worked is required to certify that "his service while so employed has been approved as satisfactory."

Regional Diabetic Services.—The standing medical committee of the Central Health Services Council has drawn up plans for a regional service for diabetics, which the Ministry of Health now commends to hospital authorities (Circular 94150/20/28, dated July 7). The plans are based on an estimate of there being three diabetics with symptoms in every 1,000 of the population of Great Britain. The plans envisage the establishment of regional centres with full facilities for the assessment and stabilization of diabetics, the treatment of emergencies, the training of patients in how to live with their disability, and regular out-patient supervision. These centres, which are regarded as being "in support of the family doctor," would be equipped with beds: 20 are thought enough for the 1,000 diabetics expected in a population of 350,000. There would also be smaller local centres for urine testing and blood-sugar estimations. Pregnant and tuberculous diabetics would need special arrangements.

Cable Code for Epidemiologists.—World Health Organization has published a new code for the cabling of information about epidemics from one part of the world to another. It is in French and English. The use of the code, which lists 135 epidemic diseases and contains 20,000 geographical names, is restricted to national health authorities and W.H.O. offices. The principal aim is to allow the rapid and direct exchange of information between governments on epidemiological matters, without the risk of it reaching unauthorized persons. The code, named "Codepid," will come into force on December 1.

Dr. W. St. C. Symmers, senior lecturer in the University of Birmingham, has been appointed to the chair of morbid anatomy of the University of London tenable at Charing Cross Hospital Medical School.

Dr. Hugo McVey, formerly Assistant Master at the Rotunda Hospital, Dublin, has been appointed Assistant Professor of Obstetrics and Gynaecology at Trinity College, Dublin.

COMING EVENTS

An Exhibition of the Medical Periodicals of the World in the Old Library at B.M.A. House will be open from 9 a.m. to 5 p.m. on Tuesday to Friday, July 21–24, and from 9 a.m. to 1 p.m. on Saturday, July 25.

Health Education.—The Central Council for Health Education has arranged a summer school in health education at Royal Holloway College, Englefield Green, Surrey, from August 10–20. The inclusive fee is £16 16s. Further details may be obtained from the Medical Director, The Central Council for Health Education, Tavistock House, Tavistock Square, London, W.C.1.

European Symposium on Cortisone.—The University of Milan has organized a European symposium on cortisone and the suprarenal cortex to be held in Milan from August 31 to September 2. The symposium will consist of several short papers on biological and clinical aspects, followed by an open discussion. For further information, communications should be addressed to Professor C. B. Ballabio, Clinica Medica dell'Università di Milano, via F. Sforza 35, Milano.

Institute of Public Administration.—The Second Health Services Conference of the Institute will be held at Church House, Westminster, from October 28 to 30. The theme of the conference will be "Making the Most of Present Resources." Speakers will include Sir Fred Messer, Professor A. Leslie Banks, Mr. Leslie Farrer-Brown, Mr. K. J. Johnson, and Mr. H. A. Goddard. Further details will be available at a later date, but inquiries should be sent to the secretary of the Institute of Public Administration, Haldane House, 76a, New Cavendish Street, London, W.1.

Military Medicine Meeting.—The sixteenth meeting of the International Committee of Military Medicine and Pharmacy will be held in Rome from October 14 to 18. Further information may be obtained from the secretary-general, 79, Rue Saint-Laurent, Liége, Belgium.

NEW ISSUES

British Journal of Industrial Medicine.—The next issue (Vol. 10, No. 3) will be available in a week's time. The contents include:

THE PRE-IMPINGER: A SELECTIVE AEROSOL SAMPLER. K. R. May and H. A. Druett.
STUDIES ON THE NATURE OF SILICOSIS. I: THE EFFECT OF SILICIC ACID ON CONNECTIVE TISSUE. P. F. Holt and Sonia G. Osborne.
THE INCIDENCE OF PEPTIC ULCER AND CHRONIC GASTRITIS AMONG SWEDISH SEA PILOTS. Tore Dalhamn.
ACUTE POISONING CAUSED BY INGESTION OF ETHYLENE CHLOROHYDRIN. F. Ballotta, P. Bertagni, and F. M. Troisi.
NIGHT WORK AND SHIFT CHANGES. S. Wyatt and R. Marriott.
LEGISLATION AND LITIGATION: COMMENTS ON THE DEVELOPMENT OF INDUSTRIAL LAW. W. Mansfield Cooper.
FROM FACTORY INSPECTION TO ADULT HEALTH SERVICE: A REVIEW OF GOVERNMENTAL ADMINISTRATION OF OCCUPATIONAL HEALTH. Milton I. Roemer.
OCCUPATIONAL HEALTH PROBLEMS OF ENGLISH PAINTERS AND VARNISHERS IN 1825. George Rosen.
PRELIMINARY NOTES ON THE TREATMENT OF TENOSYNOVITIS IN INDUSTRY. E. L. Knowles and M. D. Kipling.
AN OCCUPATIONAL HYGIENE TEAM. Peter H. Nash and R. J. Sherwood, with the assistance of Joan Bedford.
THE SEWERMAN AT WORK. Andrew Meiklejohn.
THE HEALTH OF THE ARMY. Sir Alexander Hood.

Issued quarterly; annual subscription £2 2s., single copy 12s. 6d.; obtainable from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Applications should be made first to the institution concerned.

Tuesday, July 21

MIDDLESEX COUNTY MEDICAL SOCIETY.—At Middlesex Guildhall, Westminster, S.W., 5.30 p.m., John Tate Memorial Lecture by Dr. H. M. C. Macaulay: Medicine and the Welfare State.
SOCIETY FOR THE STUDY OF ADDICTION.—At 11, Chandos Street, W., 8 p.m., Dr. J. Elkes: The So-called Hallucinogenic Drugs: An Approach to their Possible Mode of Action, and their Implications in Psychiatric Research.

Saturday, July 25

MEDICAL SOCIETY FOR THE STUDY OF VENEREAL DISEASES.—2.30 p.m., 32nd annual general meeting.

APPOINTMENTS

BLAXLAND, P. J., M.B., B.S., F.R.C.S., Surgeon Specialist, Darwin, Northern Territory, Australia.

JONES, BARBARA, M.B., Ch.B., Assistant County Medical Officer of Health, Hyde Division, Cheshire County Council.

MANCHESTER REGIONAL HOSPITAL BOARD.—S. S. Rose, M.B., Ch.B., F.R.C.S., Consultant General Surgeon to South Manchester Hospital Centre; J. B. Fawcitt, M.R.C.S., L.R.C.P., D.M.R.D., Consultant Radiologist in charge of Diagnostic Radiology Service at Crumpsall Hospital; S. H. Jackson, M.B., Ch.B., Consultant Pathologist to Ashton, Hyde and Glossop Hospitals; M. W. Johnstone, M.D., D.A., Consultant Anaesthetist to United Manchester Hospitals and Crumpsall Hospital.

NORTH-EAST METROPOLITAN REGIONAL HOSPITAL BOARD.—Helen M. Mayer, M.R.C.S., L.R.C.P., M.R.C.O.G., Part-time Consultant Gynaecologist, Metropolitan Hospital; G. L. W Bonney, M.S., F.R.C.S., Part-time Consultant Orthopaedic Surgeon, Southend-on-Sea Group of Hospitals and Runwell Hospital; C. F. Cooper, M.D., M.R.C.P., Part-time Consultant Physician, Bethnal Green Hospital.

THOMSON, KENMURE JAMES, M.B., Ch.B., D.P.H., L.M., Medical Officer of Health, Border Rural District Council and Penrith Rural District Council and Assistant County Medical Officer of Health, Cumberland.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Brown.—On June 30, 1953, at the Royal Air Force Hospital, Changi, to Marguerite, wife of Squadron-Leader T. C. Brown, of R.A.F., Tengah, Singapore, a daughter—Gillian Francis.
Kelsall.—On July 6, 1953, to Margaret, wife of A. R. Kelsall, M.D., M.R.C.P., a son—John Robert Sexton.
Keppie.—On July 4, 1953, at Billinge Maternity Hospital, near Wigan, Lancs, to Dr. Wilmott (formerly Nield-Faulkner), wife of Dr. Lawrence Scarth Keppie, of "The Poplars," Knott End-on-Sea, Fleetwood, Lancs, a son—Stuart Nield.
Otoo.—On July 5, 1953, at the Royal Infirmary, Lancaster, to Sylvia (formerly Travis), S.R.N., wife of Samuel N. Otoo, M.B., Ch.B., D.T.M.&H., of Colonial Medical Service, Gold Coast, twin sons—Michael and Christopher.

MARRIAGES

Clarkson—Daubeny.—On July 9, 1953, Patrick Wensley Clarkson, M.B.E., F.R.C.S., of 107, Harley Street, London, W., to Elizabeth Daubeny, of 49, Hill Street, London, W.

DEATHS

Cowper.—On June 28, 1953, at Estcourt, Shanklin, Isle of Wight, John Cowper, M.B., C.M., aged 91.
Munro.—On June 27, 1953, in London, Donald George Macleod Munro, M.D., M.R.C.P.Ed., aged 82.
Rawlinson.—On July 4, 1953, at the National Hospital, Queen Square, London, W.C., Ernest Goodwin Rawlinson, M.D., D.P.H., aged 76.
Rose.—On July 1, 1953, at his home, 2, The Grange, Wimbledon, London, S.W., Samuel Rose, M.B., B.S.
Waugh.—On June 25, 1953, William Waugh, L.R.C.P.&S.I. and L.M., of Maidstone House, Dover, Kent.

Any Questions?

Correspondents should give their names and addresses (not for publication) and include all relevant details in their questions, which should be typed. We publish here a selection of those questions and answers which seem to be of general interest.

Contact Lenses

Q.—*What are the indications for and against the use of contact lenses?*

A.—The chief indications for the use of contact lenses are: (1) To secure good visual acuity for certain patients who cannot see well with the aid of ordinary glasses (for example, sufferers from advanced conical cornea); (2) to enable unilateral aphakics (that is, those who, as a result of injury or after a cataract operation, have lost the lens from one eye) to secure binocular vision—an aim which is hardly ever attainable by ordinary glasses, because the aphakic eye's refraction is usually so different from that of the other eye; (3) as a protection for the cornea in certain cases of relapsing keratitis; and (4) to enable high myopes to obtain good sight without visible glasses.

Contact lenses are seldom feasible in people suffering from inflamed or irritable eyes, though a few above-mentioned cases of keratitis may stand to benefit. Nor are they suitable for infants, small or backward children, and oversensitive subjects. Sometimes a patient free from contraindications may nevertheless fail to tolerate contact lenses, even if these have been fitted with care and skill. Therefore success can never be absolutely guaranteed.

Life Expectation of Cancer Patients

Q.—*It is presumably possible to say that, if a patient has survived the treatment of a primary malignant growth for one year without a recurrence, his chances of radical cure are x%; if he has survived for two years without recurrence, his chances of cure are y% (y being greater than x); and so on. Have such figures been worked out for cancers at various sites, treated in various standard ways, and, if so, where are they to be found?*

A.—This question is hard to answer because of the difficulty which has been felt in defining what is meant by the "cure" of cancer. It is impracticable to take it to mean the complete elimination of all cancer cells from the body, because of the difficulty in knowing whether this has been successfully achieved. For example, cancer of the breast is liable to relapse after years of apparent cure, and one can never say that, in this sense, a given patient has been cured. Until recently the custom has therefore been to treat survival for five years as being the practical equivalent of a cure: if this is taken to be the definition, there are many large series which provide figures for estimating the chance of cure after one, two, or more years without recurrence.

It is, however, now generally recognized that the five-year survival rate is an inadequate index, because a considerable number of patients die of cancer more than five years after the institution of treatment (or, if untreated, after first observation) and others die of causes unconnected with cancer in less than five years. In order to overcome the difficulty, some investigators now express their results in an actuarial manner—that is to say, by comparing the number of months lived by the treated group of patients in (say) five years after treatment with the number of months which would be expected to be lived by a group of people in the general population having the same sex and age distribution; the actual number of months lived is then expressed as a percentage of the expected. In the *Survey of Cancer in London*[1] results are expressed in this way for cancer of each site and often for different methods of treatment and different stages of development of the growth. For example, radical mastectomy was followed by a five-year survival of 91% of the expected when the growth had been confined to the breast without involvement of lymph nodes, of 76% survival when the axillary nodes were involved, and of 68% when skin or muscle was also infiltrated; local mastectomy, in the same three groups, was followed by survivals of 98%, 76%, and 70% expected, and radiotherapy by survivals of 80%, 64%, and 62%.

If this idea is carried to its logical conclusion it becomes possible to define cure in a new and more practical way: that is to say, as the state of having the same expectation of life as an average representative of the general population of the same sex and age. Estimates of the chance of cure, in this sense, after different periods of survival have been worked out for a few types of cancer. The calculations involved are complex, and the basic data required to enable them to be made are not available for every site. Berkson and Gage[2] indicate one method which may be used, and give examples based on the experience of cancer of the stomach and breast treated at the Mayo Clinic. From these examples it is possible to say that the chance of cure of cancer of the breast with metastases at the time of treatment was 20% immediately after the initiation of treatment, 32% after survival for two years, 54% after survival for five years, and 85% after survival for ten years.

Boag has developed another method, based on a slightly different definition and has published, with Constance Wood,[3] detailed figures relating to the radiotherapy of oral cancer. Figures for other sites and an account of his method are given elsewhere by Boag.[4] Figures of more limited use but relating to nearly half the cancer cases occurring in the country are given by Stocks.[5] These figures relate to all the cancer cases registered in the national registration scheme, and so far results are available for survival at one and three years in the cases which were registered in 1945 and 1946.

REFERENCES
1 British Empire Cancer Campaign: *Survey of Cancer in London*, 1952.
2 *J. Amer. statist. Ass.*, 1952, 47, 501.
3 *Spec. Rep. Ser. med. Res. Coun. (Lond.)*, 1950, No. 267.
4 *J. roy. statist. Soc.*, 1949, Series B, 2, 15.
5 *Studies on Medicine and Population Subjects*, No. 3, and supplement; Cancer Registration in England and Wales. H.M.S.O., London, 1950.

Thyrotoxicosis in Pregnancy

Q.—*(1) What is the best treatment for thyrotoxicosis in pregnancy? (2) What is the prognosis if, after successful treatment, there are further pregnancies? Ought such a patient to be advised against having further children?*

A.—(1) Pregnant women with thyrotoxicosis can be treated successfully by either subtotal thyroidectomy or antithyroid drugs. In properly prepared patients there is little danger of abortion as a result of the operation. Antithyroid drugs can also be used quite safely, provided they are not given in such doses that the patient becomes hypothyroid. If the pregnant woman is overdosed with antithyroid drugs the foetal thyroid will be affected, and the baby may be born with a goitre and signs of hypothyroidism. Fortunately, thyrotoxicosis is likely to become less rather than more severe with the onset of pregnancy; hence pregnant women can usually be controlled by relatively small doses of antithyroid drugs, such as 50 mg. daily of methyl thiouracil. Doses of this order do not affect the foetal thyroid. As these drugs are excreted in the milk, breast-feeding is best avoided. Pregnant women with thyrotoxicosis should not be treated with radio-iodine, except in the first three months. After that time the foetal thyroid concentrates the isotope and it might be damaged by therapeutic doses.

(2) Thyrotoxicosis sometimes develops after the birth of a baby, although the causal connexion between the two events has not yet been clearly demonstrated. It is probably as well to advise women who have recently had thyrotoxicosis not to have a child until they have been stable for at least a year after the end of treatment. Exceptions can, however, be made in the case of women who are particularly anxious to have a child, even if previous pregnancies have appeared to precipitate thyrotoxicosis, since there is no great difficulty in dealing with thyrotoxicosis during pregnancy.

Read's Formula for B.M.R.*

Q.—*How reliable is Read's formula for calculating the basal metabolic rate? How does it compare with clinical findings for controlling thyroid therapy in myxoedema and in the diagnosis of thyroid disease?*

A.—Read's formula for calculating the basal metabolic rate cannot be considered to be reliable, for it closely approximates to the actual figure in only slightly more than half of the cases. It does not compare favourably with clinical findings in determining the maintenance dose of thyroid in myxoedema; the improvement in the patient's mental and physical state is by far the best index for assessing the effectiveness of treatment. In the diagnosis of thyroid disease reliance should be placed on the clinical findings rather than on a formula.

Hemiplegic Migraine

Q.—*What prognostic significance has an attack of hemiplegic migraine in a young man who for a number of years has been subject to attacks of ordinary migraine?*

A.—Hemiplegic migraine usually means an attack which starts with hemiplegia and possibly sensory impairment on the same side, and if the hemiplegia is right-sided frequently dysphasia as well; headache of migrainous type starts soon after the onset of the hemiplegia. This type of migraine, which is rare, tends to occur in families, and it is usual for the hemiplegia to disappear completely in a period of a few hours up to three days. It is probable that the cause of the hemiplegia is vasoconstriction of cerebral arteries. In rare cases a permanent hemianopia may follow an attack of migraine with a hemianopic aura, and it is conceivable that permanent hemiplegia might follow an attack of hemiplegic migraine. An intracranial angioma can cause a similar clinical picture: if two or more attacks occur with the hemiplegia on the same side in each attack, radiography of the skull and carotid arteriography are advisable. The subject of migrainous variants, including hemiplegic migraine, was discussed recently in the Annual Oration to the Medical Society of London by Sir Charles Symonds.[1]

REFERENCE

[1] *Trans. med. Soc. Lond.*, 1952, 67, 237.

Apical Infection

Q.—*Can apical dental infection be confidently excluded by methods of examination other than radiography? If so, please state briefly what they are.*

A.—Apical dental infection can be confidently excluded without the use of radiographs when the teeth concerned can be shown to be vital and the gum tissue is healthy with no pockets around the necks of the teeth.

Vitality tests are carried out by the application of heat, cold, or the electrical pulp-tester, for increasing periods of time until a response is felt. Heat is most conveniently applied by means of a heated piece of gutta-percha mounted on a dental instrument; cold by a pledget of cotton-wool saturated with ethyl chloride which is allowed to evaporate until a frost appears on the surface. A careful comparison with another tooth is necessary, because patients vary considerably in their sensitivity to these tests. Sometimes perfectly healthy pulps fail to give a response at all, and then a radiograph is necessary. An infected pulp can give a response so long as some vital tissue remains, but such a tooth will usually have caused pain.

The condition of the gum and underlying bone is important, because in paradontal disease infection may reach the apex of a tooth from a deep pocket between the tooth and the gum. If therefore the gum has lost its normal pale pink stippled appearance and bleeds readily when examined with a blunt probe to see whether a pocket exists, a radiograph is necessary to eliminate disease of the alveolar process.

*Read's formula: 0.75 (pulse rate + 0.74 pulse pressure) − 72 = basal metabolic rate.

Paget's Disease and Vitamin B_{12}

Q.—*A patient of mine alleges that injections of vitamin B_{12} have kept his Paget's disease (osteitis deformans) under control for at least three years. Is there any rational basis for this claim?*

A.—There is no rational basis for this claim. Paget's disease may remain symptomless and quiescent for a long time without any treatment at all.

Midge Repellents

Q.—*What measures of protection against attack by midges can be advised to a lady who has developed a skin sensitivity to dimethyl phthalate and wishes to spend much time out of doors?*

A.—Control of midges is difficult because our knowledge of their breeding grounds is comparatively small: the indications are that they breed over large areas of moist or swampy ground. It is usual, therefore, to rely on repellents for protection. A person allergic to dimethyl phthalate might try other substances—for example, oil of citronella or pyrethrum extract. These can be made up into an ointment by admixture with petroleum jelly. Other synthetic repellents, such as "indalone," 2-ethyl,1-3 hexanediol, or the Swiss preparation "kik," may be difficult to obtain in this country.

Should the sufferer prove sensitive to any type of repellent applied directly to the skin she might try a wide-mesh veil, impregnated with undiluted dimethyl phthalate and worn attached to the brim of a hat. A suitable material would be green rot-proof netting with a mesh of 4/16 × 5/16 in. (6.35 × 7.94 mm.). If this is kept in a tin when not in use, one impregnation should last a fortnight. For protection of the legs, cotton stockings smeared with dimethyl phthalate might be effective and harmless.

NOTES AND COMMENTS

Absence of Axillary Hair in a Man.—Mr. H. MILNES WALKER (Crewe) writes: The advice to the young man embarrassed by the absence of axillary hair ("Any Questions?" June 27, p. 1460) is as good an example of fussy medication as one could wish to come across. It should not be beyond the wit of a sympathetic doctor to implant in his mind that most of us have some oddity or other that we should learn to ignore together with the occasional comment it may invite: surely better than the implantation into his body of a hormone that may produce in him effects as alarming as the absence of axillary hair. What young man would not rather be athletic though hairless under the arms than blessed with the hairiness of Esau and useless on the playing-fields?

Correction.—The paper on the genetics of infantile amaurotic idiocy referred to in "Any Questions?" last week (July 11, p. 107) was by D. Slome.

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